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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 3	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 4	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6	Mar 08	Gene Names now available in BIOSIS
NEWS 7	Mar 22	TOXLIT no longer available
NEWS 8	Mar 22	TRCTHERMO no longer available
NEWS 9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 10	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY
NEWS 11	Apr 02	PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS 12	Apr 08	"Ask CAS" for self-help around the clock
NEWS 13	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 14	Apr 09	ZDB will be removed from STN
NEWS 15	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 16	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 18	Apr 22	Federal Research in Progress (FEDRIP) now available

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 18:43:32 ON 01 MAY 2002

=> file medline, uspatful, dgene, embase, biotechds, frosti, fsta

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 18:44:03 ON 01 MAY 2002

FILE 'USPATFULL' ENTERED AT 18:44:03 ON 01 MAY 2002
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=> s kininogen

L1 4339 KININOGEN

=> s angiogenesis

L2 90365 ANGIOGENESIS

=> s l2 and inhibition

L3 15312 L2 AND INHIBITION

=> s l3 and compositon

L4 5 L3 AND COMPOSITON

=> d l4 ti abs ibib tot

L4 ANSWER 1 OF 5 USPATFULL
TI Gene sequence variances in genes related to folate metabolism having utility in determining the treatment of disease
AB The present disclosure describes the use of genetic variance information for folate transport or metabolism genes or pyrimidine transport or metabolism genes in the selection of effective methods of treatment of a disease or condition. The variance information is indicative of the expected response of a patient to a method of treatment. Methods of determining relevant variance information and additional methods of using such variance information are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:72850 USPATFULL
TITLE: Gene sequence variances in genes related to folate metabolism having utility in determining the treatment of disease
INVENTOR(S): Stanton, Vincent P., JR., Belmont, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002039990	A1	20020404
APPLICATION INFO.:	US 2000-733651	A1	20001207 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-710768, filed on 8 Nov 2000, PENDING Continuation-in-part of Ser. No. US 2000-696634, filed on 24 Oct 2000, PENDING Continuation-in-part of Ser. No. US 2000-684359, filed on 6 Oct 2000, PENDING Continuation-in-part of Ser. No. US 2000-638267, filed on 14 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-596033, filed on 15 Jun 2000, ABANDONED Continuation-in-part of Ser. No. US 1999-357743, filed on 20 Jul 1999, ABANDONED Continuation-in-part of Ser. No. US 1999-357024, filed on 19 Jul 1999, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-93484P	19980720 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ANITA L. MEIKLEJOHN, PH.D., FISH & RICHARDSON P.C., 225 Franklin Street, Boston, MA, 02110-2804
NUMBER OF CLAIMS: 119
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 7986
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 2 OF 5 USPATFULL
TI Anti-cancer therapy agent of arsenic hexoxide (As4O6) of a natural chemical substance and its pharmaceutical composition
AB This invention is about the identification of the HD-2, a natural chemical substance that was separated and purified from a natural product, Sinsuk, as arsenic hexoxide (As.sub.4O.sub.6) and about its therapeutic efficacy as an anti-cancer drug and pharmaceutical composition. Arsenic hexoxide (As.sub.4O.sub.6), a natural chemical substance obtained from Sinsuk after eliminating the toxic property, has a potent anti-cancer efficacy by its direct cytotoxicity on tumor cells and suppresses the formation of new blood vessels of tumor masses, which results in complete cure of malignant cancers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2002:48062 USPATFULL
TITLE: Anti-cancer therapy agent of arsenic hexoxide (As4O6) of a natural chemical substance and its pharmaceutical composition
INVENTOR(S): Bae, Ill-Ju, Seoul, KOREA, REPUBLIC OF
Kim, Jong-Bae, Pohang-city, KOREA, REPUBLIC OF
Eun, Choong-Ki, Pusan-city, KOREA, REPUBLIC OF
Song, Seung-Kyu, Pohang-city, KOREA, REPUBLIC OF
Suh, Byung-Sun, Pohang-city, KOREA, REPUBLIC OF
Lee, Kwan-Hee, Pohang-city, KOREA, REPUBLIC OF

Doo, Myoung-Sool, Pohang-city, KOREA, REPUBLIC OF
Kwak, Jin-Hwan, Pohang-city, KOREA, REPUBLIC OF
Yong, Byung-Doo, Pohang-city, KOREA, REPUBLIC OF
Yoon, Taek-Joon, Koyang-city, KOREA, REPUBLIC OF
Kang, Tae-Bong, Pohang-city, KOREA, REPUBLIC OF
Park, Choon-Ho, Pohang-city, KOREA, REPUBLIC OF

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002028253	A1	20020307
APPLICATION INFO.:	US 2001-951393	A1	20010914 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-105086, filed on 26 Jun 1998, GRANTED, Pat. No. US 6309672

	NUMBER	DATE
PRIORITY INFORMATION:	KR 1998-16486	19980508

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Gary M. Nath, Nath & Associates PLLC, 6th Floor, 1030 15th Street, N.W., Washington, DC, 20005
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 971
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 3 OF 5 USPATFULL
TI Somatostatin antagonists
AB The invention features somatostatin antagonists having a D-amino acid at
the second residue.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2001:112494 USPATFULL
TITLE: Somatostatin antagonists
INVENTOR(S): Coy, David H., New Orleans, LA, United States
Morgan, Barry, Franklin, MA, United States
Murphy, William, Slidell, LA, United States
PATENT ASSIGNEE(S): Biomeasure Incorporated, Milford, MA, United States (U.S. corporation)
The Administration of the Tulane Educational Fund, New Orleans, LA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6262229	B1	20010717
APPLICATION INFO.:	US 1997-855204		19970513 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-32358P	19961204 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Cintins, Marianne M.
ASSISTANT EXAMINER: Delacroix-Muirheid, C.
LEGAL REPRESENTATIVE: Conway, John D., Morrill, Brian R.Fish & Richardson
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
LINE COUNT: 1228
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 4 OF 5 USPATFULL
TI Urokinase-type plasminogen activator receptor

AB Activation of plasminogen to plasmin is inhibited by preventing the binding of a receptor binding form of urokinase-type plasminogen activator to a urokinase-type plasminogen activator receptor in a mammal, thereby preventing the urokinase-type plasminogen activator from converting plasminogen into plasmin. DNA fragments which encode for soluble, active fragments of the urokinase-type plasminogen activator receptor are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2001:93478 USPATFULL
TITLE:	Urokinase-type plasminogen activator receptor
INVENTOR(S):	Dan.o slashed. , Keld, Charlottenlund, Denmark Blasi, Francesco, Charlottenlund, Denmark Roldan, Ann Louring, Vallensb.ae butted.k, Denmark Cubellis, Maria Vittoria, Naples, Italy Masucci, Maria Teresa, Naples, Italy Appella, Ettore, Chevy Chase, MD, United States Schleuning, W.D., Berlin, Germany, Federal Republic of Behrendt, Niels, Bagsv.ae butted.rd, Denmark R.o slashed.nne, Ebbe, Copenhagen, Denmark Kristensen, Peter, Copenhagen, Denmark Pollanen, Jari, Espoo, Finland Salonen, Eeva-Marjatta, Espoo, Finland Stephens, Ross W., Vantaa, Finland Tapiovaara, Hannele, Helsinki, Finland Vaheri, Antti, Kauniainen, Finland M.o slashed.ller, Lisbeth Birk, Bagsv.ae butted.rd, Denmark Ellis, Vincent, Copenhagen, Denmark Lund, Leif R.o slashed.ge, Copenhagen, Denmark Ploug, Michael, Copenhagen, Denmark Pyke, Charles, S.o slashed.borg, Denmark Patthy, Laszlo, Budapest, Hungary
PATENT ASSIGNEE(S):	Cancerforskningsfondet af 1989, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6248712	B1	20010619
APPLICATION INFO.:	US 1995-442108		19950516 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-319052, filed on 6 Oct 1994, now patented, Pat. No. US 5891644 Continuation of Ser. No. US 824189, now abandoned Continuation-in-part of Ser. No. US 1989-374854, filed on 3 Jul 1989, now abandoned Continuation-in-part of Ser. No. US 1989-334613, filed on 7 Apr 1989, now abandoned

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Feisee, Lila
ASSISTANT EXAMINER:	Basi, Nirmal S.
LEGAL REPRESENTATIVE:	Cooper, Iver P.
NUMBER OF CLAIMS:	28
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	86 Drawing Figure(s); 54 Drawing Page(s)
LINE COUNT:	6444

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 5 OF 5 USPATFULL

TI Vectors and methods for recombinant production of uPA-binding fragments of the human urokinase-type plasminogen receptor (uPAR)

AB Activation of plasminogen to plasma is inhibited by preventing the binding of a receptor binding form of urokinase-type plasminogen

activator to a urokinase-type plasminogen activator receptor in a mammal, thereby preventing the urokinase-type plasminogen activator from converting plasminogen into plasmin. DNA fragments which encode for soluble, active fragments of the urokinase-type plasminogen activator are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	1999:43412 USPATFULL
TITLE:	Vectors and methods for recombinant production of uPA-binding fragments of the human urokinase-type plasminogen receptor (uPAR)
INVENTOR(S):	Dan.o slashed. , Keld, Charlottenlund, Denmark Blasi, Francesco, Charlottenlund, Denmark Roldan, Ann Louring, Vallensb.ae butted.k, Denmark Cubellis, Maria Vittoria, Napoli, Italy Masucci, Maria Teresa, Napoli, Italy Appella, Ettore, Chevy Chase, MD, United States Schleuning, Wolf-Dieter, Berlin, Germany, Federal Republic of Behrendt, Niels, Bagsv.ae butted.rd, Denmark R.o slashed.nne, Ebbe, Copenhagen, Denmark Kristensen, Peter, Copenhagen, Denmark Pollanen, Jari, Espoo, Finland Salonen, Eeva-Marjatta, Espoo, Finland Stephens, Ross W., Helsinki, Finland Tapiovaara, Hannele, Helsinki, Finland Vaheri, Antti, Kauniainen, Finland M.o slashed.ller, Lisbeth Birk, Bagsv.ae butted.rd, Denmark Ellis, Vincent, Copenhagen, Denmark Lund, Leif R.o slashed.ge, Copenhagen, Denmark Ploug, Michael, Copenhagen, Denmark Pyke, Charles, S.o slashed.borg, Denmark Patthy, Laszlo, Budapest, Hungary
PATENT ASSIGNEE(S):	Cancerforskningsfondet af 1989, Copenhagen K, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5891664		19990406
APPLICATION INFO.:	US 1994-319052		19941006 (8)

RELATED APPLN. INFO.:	Continuation of Ser. No. US 1991-824189, filed on 6 Dec 1991, now abandoned which is a continuation-in-part of Ser. No. US 1989-374854, filed on 3 Jul 1989, now abandoned which is a continuation-in-part of Ser. No. US 1989-334613, filed on 7 Apr 1989, now abandoned
DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Walsh, Stephen G.
ASSISTANT EXAMINER:	Fitzgerald, David L.
LEGAL REPRESENTATIVE:	Cooper, Iver P.
NUMBER OF CLAIMS:	22
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	83 Drawing Figure(s); 53 Drawing Page(s)
LINE COUNT:	6449

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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(FILE 'HOME' ENTERED AT 18:43:32 ON 01 MAY 2002)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, BIOTECHDS, FROSTI, FSTA' ENTERED
AT 18:44:03 ON 01 MAY 2002
L1 4339 S KININOGEN
L2 90365 S ANGIOGENESIS
L3 15312 S L2 AND INHIBITION
L4 5 S L3 AND COMPOSITON

=> s l3 and composition

L5 2358 L3 AND COMPOSITION

=> s l5 and glycine

L6 890 L5 AND GLYCINE

=> s l7 and histidine

L7 NOT FOUND
The L-number entered could not be found. To see the definition of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l6 and histidine

L7 468 L6 AND HISTIDINE

=> s l7 and lysine

L8 424 L7 AND LYSINE

=> s l8 and PHE

L9 295 L8 AND PHE

=> s l9 and protecting group

L10 53 L9 AND PROTECTING GROUP

=> d l10 ti abs ibib 1-10

L10 ANSWER 1 OF 53 USPATFULL
TI .beta.-sheet mimetics and methods relating to the use thereof
AB .beta.-sheet mimetics and methods relating to the same are disclosed. The .beta.-sheet mimetics have utility as protease and kinase inhibitors, as well as inhibitors of transcription factors and protein-protein binding interactions. Methods of the invention include administration of a .beta.-sheet mimetic, or use of the same for the manufacture of a medicament for treatment of a variety of conditions associated with the targeted protease, kinase, transcription factor and/or protein-protein binding interaction.

ACCESSION NUMBER: 2002:81487 USPATFULL
TITLE: .beta.-sheet mimetics and methods relating to the use thereof
INVENTOR(S): Qabar, Maher N., Redmond, WA, United States
McMillan, Michael K., Bellevue, WA, United States
Kahn, Michael S., Kirkland, WA, United States
Tulinsky, John E., Seattle, WA, United States
Ogbu, Cyprian O., Bellevue, WA, United States
Mathew, Jessymol, Bellevue, WA, United States
PATENT ASSIGNEE(S): Molecumetics Ltd., Bellevue, WA, United States (U.S. corporation)

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NEWS 4	Feb 24	TEMA now available on STN
NEWS 5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 6	Feb 26	PCTFULL now contains images
NEWS 7	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 8	Mar 24	PATDPAFULL now available on STN
NEWS 9	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 10	Apr 11	Display formats in DGENE enhanced
NEWS 11	Apr 14	MEDLINE Reload
NEWS 12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 13	AUG 22	Indexing from 1927 to 1936 added to records in CA/CAPLUS
NEWS 14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 15	Apr 28	RDISCLOSURE now available on STN
NEWS 16	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 17	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 18	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 19	May 19	Simultaneous left and right truncation added to WSCA
NEWS 20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 22	Jun 06	PASCAL enhanced with additional data
NEWS 23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 24	Jun 25	HSDB has been reloaded
NEWS 25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS 26	Jul 21	Identification of STN records implemented
NEWS 27	Jul 21	Polymer class term count added to REGISTRY
NEWS 28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS 29	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS 30	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 31	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS 32	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS 33	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS 34	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS 35	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS 36	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS 37	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Right Truncation

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 NEWS 38  AUG 18  Simultaneous left and right truncation added to ANABSTR

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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=> file medline, uspatful, dgene, fsta, jicst, wpids
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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FILE 'WPIDS' ENTERED AT 18:11:41 ON 02 SEP 2003
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=> s pharmaceutical composition
L1      103614 PHARMACEUTICAL COMPOSITION

=> s l1 and His-Lys-Phe-Lys
L2           13 L1 AND HIS-LYS-PHE-LYS

=> d l2 ti abs ibib tot

L2   ANSWER 1 OF 13  USPATFULL on STN
TI     SECRETED PROTEINS AND POLYNUCLEOTIDES ENCODING THEM
AB     Novel polynucleotides and the proteins encoded thereby are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER:         2003:141109  USPATFULL
TITLE:                    SECRETED PROTEINS AND POLYNUCLEOTIDES ENCODING THEM
INVENTOR(S):              JACOBS, KENNETH, NEWTON, MA, UNITED STATES
                          MCCOY, JOHN M., READING, MA, UNITED STATES
                          LAVALLIE, EDWARD R., HARVARD, MA, UNITED STATES
```

COLLINS-RACIE, LISA A., ACTON, MA, UNITED STATES
MERBERG, DAVID, ACTON, MA, UNITED STATES
AGOSTINO, MICHAEL J., ANDOVER, MA, UNITED STATES
STEININGER, ROBERT, II, CAMBRIDGE, MA, UNITED STATES
SPAULDING, VIKKI, BILLERICA, MA, UNITED STATES
WONG, GORDON G., BROOKLINE, MA, UNITED STATES
CLARK, HILARY F., SAN FRANCISCO, CA, UNITED STATES
FECHTEL, KIM, ARLINGTON, MA, UNITED STATES
EVANS, CHERYL, GERMANTOWN, MD, UNITED STATES
TREACY, MAURICE, DUBLIN, IRELAND

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003096951	A1	20030522	
APPLICATION INFO.:	US 1999-374046	A1	19990813	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-96622P	19980814	(60)
	US 1998-96815P	19980817	(60)
	US 1998-99229P	19980904	(60)
	US 1998-105368P	19981023	(60)
	US 1999-115234P	19990108	(60)
	US 1999-119931P	19990212	(60)
	US 1999-120575P	19990218	(60)
	US 1999-132020P	19990430	(60)
	US 1999-148424P	19990811	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 22385
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 2 OF 13 USPATFULL on STN
TI Novel human leucine-rich repeat containing protein expressed predominately in small intestine, HLRRSI1
AB The present invention provides novel polynucleotides encoding HLRRSI1 polypeptides, fragments and homologues thereof. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and therapeutic methods for applying these novel HLRRSI1 polypeptides to the diagnosis, treatment, and/or prevention of various diseases and/or disorders related to these polypeptides, particularly gastrointestinal diseases and/or disorders. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2003:23722 USPATFULL
TITLE: Novel human leucine-rich repeat containing protein expressed predominately in small intestine, HLRRSI1
INVENTOR(S): Feder, John N., Belle Mead, NJ, UNITED STATES
Ramanathan, Chandra S., Wallingford, CT, UNITED STATES
Mintier, Gabriel A., Hightstown, NJ, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003017562	A1	20030123	
APPLICATION INFO.:	US 2001-29347	A1	20011220	(10)

	NUMBER	DATE

PRIORITY INFORMATION:	US 2000-257774P 20001222 (60)
DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS:	23
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	9 Drawing Page(s)
LINE COUNT:	14217

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 3 OF 13 USPATFULL on STN

TI 31 human secreted proteins

AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:4280 USPATFULL
TITLE:	31 human secreted proteins
INVENTOR(S):	Rosen, Craig A., Laytonsville, MD, UNITED STATES Ruben, Steven M., Olney, MD, UNITED STATES Ferrie, Ann M., Tewksbury, MA, UNITED STATES Florence, Charles, Rockville, MD, UNITED STATES Young, Paul E., Gaithersburg, MD, UNITED STATES Yu, Guo-Liang, Berkeley, CA, UNITED STATES Ni, Jian, Rockville, MD, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003004324	A1	20030102
APPLICATION INFO.:	US 2001-798889	A1	20010306 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1999-393022, filed on 9 Sep 1999, ABANDONED Continuation-in-part of Ser. No. WO 1999-US5721, filed on 11 Mar 1999, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-77714P	19980312 (60)
	US 1998-77686P	19980312 (60)
	US 1998-77687P	19980312 (60)
	US 1998-77696P	19980312 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
NUMBER OF CLAIMS:	23
EXEMPLARY CLAIM:	1
LINE COUNT:	12188

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 4 OF 13 USPATFULL on STN

TI Compositions and methods relating to lung specific genes and proteins

AB The present invention relates to newly identified nucleic acids and polypeptides present in normal and neoplastic lung cells, including fragments, variants and derivatives of the nucleic acids and polypeptides. The present invention also relates to antibodies to the polypeptides of the invention, as well as agonists and antagonists of the polypeptides of the invention. The invention also relates to

compositions comprising the nucleic acids, polypeptides, antibodies, variants, derivatives, agonists and antagonists of the invention and methods for the use of these compositions. These uses include identifying, diagnosing, monitoring, staging, imaging and treating lung cancer and non-cancerous disease states in lung, identifying lung tissue, monitoring and identifying and/or designing agonists and antagonists of polypeptides of the invention. The uses also include gene therapy, production of transgenic animals and cells, and production of engineered lung tissue for treatment and research.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2002:323329 USPATFULL			
TITLE:	Compositions and methods relating to lung specific genes and proteins			
INVENTOR(S):	Macina, Roberto, San Jose, CA, UNITED STATES Recipon, Herve A., San Francisco, CA, UNITED STATES Chen, Sei-Yu, Foster City, CA, UNITED STATES Sun, Yongming, San Jose, CA, UNITED STATES Liu, Chenghua, San Jose, CA, UNITED STATES			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002183500	A1	20021205	
APPLICATION INFO.:	US 2001-1857	A1	20011120	(10)
	NUMBER		DATE	
PRIORITY INFORMATION:	US 2000-252054P		20001120	(60)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	APPLICATION			
LEGAL REPRESENTATIVE:	LICATLA & TYRRELL P.C., 66 E. MAIN STREET, MARLTON, NJ, 08053			
NUMBER OF CLAIMS:	17			
EXEMPLARY CLAIM:	1			
LINE COUNT:	9589			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 5 OF 13 USPATFULL on STN

TI 23927, a novel human ion channel

AB The invention provides isolated nucleic acids molecules, designated 23927 or IC23927 nucleic acid molecules, which encode ion channel molecules. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing IC23927 nucleic acid molecules, host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which an IC23927 gene has been introduced or disrupted. The invention still further provides isolated IC23927 proteins, fusion proteins, antigenic peptides and anti-IC23927 antibodies. Diagnostic methods utilizing compositions of the invention are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2002:308330 USPATFULL			
TITLE:	23927, a novel human ion channel			
INVENTOR(S):	Curtis, Rory A. J., Southborough, MA, UNITED STATES Silos-Santiago, Inmaculada, Cambridge, MA, UNITED STATES			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002173455	A1	20021121	
APPLICATION INFO.:	US 2001-796720	A1	20010228	(9)
	NUMBER		DATE	

PRIORITY INFORMATION: US 2000-185938P 20000229 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 5097
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 6 OF 13 USPATFULL on STN
TI CD16-II variants
AB Human CD16-II variants, DNA sequences coding for them, their use in therapy and/or in diagnosis of autoimmune diseases and inflammatory illnesses, as well as pharmaceutical compositions comprising them, are disclosed. The sequence listing for the new polypeptides is provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2002:224701 USPATFULL
TITLE: CD16-II variants
INVENTOR(S): Luo, Shun, Needham, MA, United States
PATENT ASSIGNEE(S): Applied Research Systems ARS Holding N.V., NETHERLANDS ANTILLES (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6444789	B1	20020903	
APPLICATION INFO.:	US 1995-433123		19950503	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Ulm, John
LEGAL REPRESENTATIVE: Browdy and Neimark, P.L.L.C.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 1004
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 7 OF 13 USPATFULL on STN
TI Secreted proteins and polynucleotides encoding them
AB Novel polynucleotides and the proteins encoded thereby are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2002:126876 USPATFULL
TITLE: Secreted proteins and polynucleotides encoding them
INVENTOR(S): Jacobs, Kenneth, Newton, MA, UNITED STATES
McCoy, John M., Reading, MA, UNITED STATES
LaVallie, Edward R., Harvard, MA, UNITED STATES
Collins-Racie, Lisa A., Acton, MA, UNITED STATES
Evans, Cheryl, Germantown, MD, UNITED STATES
Merberg, David, Acton, MA, UNITED STATES
Treacy, Maurice, Dun Laoghaire, IRELAND
Spaulding, Vikki, Lowell, MA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002065394	A1	20020530	
APPLICATION INFO.:	US 2000-745763	A1	20001222	(9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1998-40963, filed on 18 Mar 1998, UNKNOWN
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
NUMBER OF CLAIMS: 264

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 17713
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 8 OF 13 USPATFULL on STN
TI Size-variable strain-specific protective antigen for potomac horse fever
AB An isolated and purified antigen which is expressed by a wild-type E. risticii strain and is specific to the strain. The present invention also relates to nucleic acid constructs which encode the antigen, expression vectors, transformed host cells, and methods for producing the antigen.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2002:87998 USPATFULL
TITLE: Size-variable strain-specific protective antigen for potomac horse fever
INVENTOR(S): Dutta, Sukanta, Glenn Dale, MD, United States
Biswas, Biswajit, Greenbelt, MD, United States
Vemulapalli, Ramesh, Blacksburg, VA, United States
PATENT ASSIGNEE(S): University of Maryland College Park, College Park, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6375954	B1	20020423	
APPLICATION INFO.:	US 1998-157257		19980918	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1997-59252P	19970918	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Graser, Jennifer E.
LEGAL REPRESENTATIVE: Arent Fox Kintner Plotkin Kahn PLLC
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 2907
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 9 OF 13 USPATFULL on STN
TI Cell division regulators
AB The invention provides three human cell division regulators (HCDR) and polynucleotides which identify and encode HCDR. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for preventing and treating disorders associated with expression of HCDR.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2000:124797 USPATFULL
TITLE: Cell division regulators
INVENTOR(S): Hillman, Jennifer L., Mountain View, CA, United States
Bandman, Olga, Mountain View, CA, United States
Lal, Preeti, Sunnyvale, CA, United States
Shah, Purvi, Sunnyvale, CA, United States
Corley, Neil C., Mountain View, CA, United States
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6121019		20000919	
APPLICATION INFO.:	US 1999-274570		19990323	(9)

RELATED APPLN. INFO.: Division of Ser. No. US 1998-165234, filed on 1 Oct 1998, now patented, Pat. No. US 5928899 which is a division of Ser. No. US 1997-951148, filed on 15 Oct 1997, now patented, Pat. No. US 5871973
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Achutamurthy, Ponnathapu
ASSISTANT EXAMINER: Mayhew, Bradley S.
LEGAL REPRESENTATIVE: Incyte Pharmaceuticals, Inc.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 26 Drawing Figure(s); 26 Drawing Page(s)
LINE COUNT: 3015
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 10 OF 13 USPATFULL on STN
TI Zinc ring protein
AB The invention provides a human zinc RING protein (ZIRI) and polynucleotides which identify and encode ZIRI. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for treating disorders associated with expression of ZIRI.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 1999:159988 USPATFULL
TITLE: Zinc ring protein
INVENTOR(S): Hillman, Jennifer L., Mountain View, CA, United States
Lal, Preeti, Sunnyvale, CA, United States
Shah, Purvi, Sunnyvale, CA, United States
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5998372		19991207
APPLICATION INFO.:	US 1998-128369		19980803 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1997-867057, filed on 2 Jun 1997, now patented, Pat. No. US 5840555, issued on 24 Nov 1998
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Wax, Robert A.
ASSISTANT EXAMINER: Monshipouri, Maryam
LEGAL REPRESENTATIVE: Incyte Pharmaceuticals, Inc., Mohan-Peterson, Sheela
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 2338
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 11 OF 13 USPATFULL on STN
TI CD16-II variants
AB Human CD16-II variants, DNA sequences coding for them, their use in therapy and/or in diagnosis of autoimmune diseases and inflammatory illnesses, as well as pharmaceutical compositions comprising them, are disclosed. The sequence listing for the new polypeptides is provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 1999:159782 USPATFULL
TITLE: CD16-II variants
INVENTOR(S): Luo, Shun, Needham, MA, United States
PATENT ASSIGNEE(S): Applied Research Systems ARS Holding N.V., Curacao, Netherlands (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5998166		19991207
APPLICATION INFO.:	US 1996-667939		19960624 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1995-433123, filed on 3 May 1995
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Hutzell, Paula K.
ASSISTANT EXAMINER: Lazar-Wesley, Elaine
LEGAL REPRESENTATIVE: Browdy and Neimark
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 1143
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 12 OF 13 USPATFULL on STN
TI Polynucleotides encoding human brain phosphodiesterase
AB Isolated cDNA clones from human brain (frontal cortex) cDNA libraries that encode a unique subtype of the low K.sub.m, cAMP-specific phosphodiesterases (PDE IVs) are disclosed. Analysis of the distribution of hPDE IV.sub.B mRNA expression in various human tissues using a nonconserved fragment of the cDNA as a probe revealed a restricted pattern of expression, with an .about.4-kb MRNA detected in brain, heart, lung and skeletal muscle and not in placenta, liver, kidney or pancreas. Furthermore, an additional .about.5-kb hPDE IV.sub.B.sup.-related mRNA species was detected in brain tissue. Expression of hPDE IV.sub.B in a genetically-engineered PDE-deficient strain of the yeast Saccharomyces cerevisiae resulted in the overproduction of cAMP PDE activity which displayed the expected kinetic characteristics for a PDE IV: 1) low K.sub.m (4.3 .mu.M) for cAMP, 2) high K.sub.m (>3 mM) for cGMP, and 3) sensitivity to rolipram (K.sub.i =0.085 .mu.M), a selective inhibitor of PDE IV. Recombinant HPDE IV.sub.B also bound [.sup.3 H]R-rolipram saturably and with a high affinity. Analysis of [.sup.3 H]R-rolipram binding data revealed curvilinear Scatchard plots, suggesting the presence of two non-interacting high affinity rolipram binding sites (K.sub.d =0.4 and 6 nM) or a negatively cooperative interaction among multiple binding sites. This novel enzyme is particularly useful for screening candidate compounds for their ability to serve as potential anti-depressant, antiasthmatic or anti-inflammatory agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 1999:89054 USPATFULL
TITLE: Polynucleotides encoding human brain phosphodiesterase
INVENTOR(S): Livi, George P., Havertown, PA, United States
McLaughlin, Megan M., Drexel Hill, PA, United States
Torphy, Theodore J., Bryn Mawr, PA, United States
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5932477		19990803
APPLICATION INFO.:	US 1997-942521		19971002 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 446386
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Elliott, George C.
ASSISTANT EXAMINER: Brusca, John S.
LEGAL REPRESENTATIVE: Hecht, Elizabeth T., Gimmi, Edward R., King, William T.
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 7 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT: 1649
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 13 OF 13 USPATFULL on STN
TI Cell division regulators
AB The invention provides three human cell division regulators (HCDR) and polynucleotides which identify and encode HCDR. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for preventing and treating disorders associated with expression of HCDR.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 1999:85250 USPATFULL
TITLE: Cell division regulators
INVENTOR(S): Hillman, Jennifer L., Mountain View, CA, United States
Bandman, Olga, Mountain View, CA, United States
Lal, Preeti, Sunnyvale, CA, United States
Shah, Purvi, Sunnyvale, CA, United States
Corley, Neil C., Mountain View, CA, United States
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5928899		19990727
APPLICATION INFO.:	US 1998-165234		19981001 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1997-951148, filed on 15 Oct 1997
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Wax, Robert A.
ASSISTANT EXAMINER: Mayhew, Bradley S.
LEGAL REPRESENTATIVE: Incyte Pharmaceuticals, Inc.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 26 Drawing Figure(s); 26 Drawing Page(s)
LINE COUNT: 2866
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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NEWS	4	Feb 16	TOXLINE no longer being updated
NEWS	5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS	6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS	7	May 07	DGENE Reload
NEWS	8	Jun 20	Published patent applications (A1) are now in USPATFULL
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=> s angiogenesis

L1 111516 ANGIOGENESIS

=> s l1 and inhibition

L2 20392 L1 AND INHIBITION

=> s l2 and peptide

L3 6317 L2 AND PEPTIDE

=> s kininogen

L4 10807 KININOGEN

=> s l3 and l4

L5 19 L3 AND L4

=> d l19 ti abs ibib tot

L19 NOT FOUND
The L-number entered [redacted] not been defined in this sess , or it has been deleted. To see the L-numbers currently defined in this session, enter DISPLAY HISTORY at an arrow prompt (=>).

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L5 ANSWER 1 OF 19 MEDLINE
TI Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and inhibits **angiogenesis**: partial activity within domain 5.
AB We previously reported that the binding of two-chain high molecular weight **kininogen** (HKa) to endothelial cells may occur through interactions with endothelial urokinase receptors. Since the binding of urokinase to urokinase receptors activates signaling responses and may stimulate mitogenesis, we assessed the effect of HKa binding on endothelial cell proliferation. Unexpectedly, HKa inhibited proliferation in response to several growth factors, with 50% **inhibition** caused by approximately 10 nM HKa. This activity was Zn(2+) dependent and not shared by either single-chain high molecular weight **kininogen** (HK) or low molecular weight **kininogen**. HKa selectively inhibited the proliferation of human umbilical vein and dermal microvascular endothelial cells, but did not affect that of umbilical vein or human aortic smooth muscle cells, trophoblasts, fibroblasts, or carcinoma cells. **Inhibition** of endothelial proliferation by HKa was associated with endothelial cell apoptosis and unaffected by antibodies that block the binding of HK or HKa to any of their known endothelial receptors. Recombinant HK domain 5 displayed activity similar to that of HKa. In vivo, HKa inhibited neovascularization of subcutaneously implanted Matrigel plugs, as well as rat corneal **angiogenesis**. These results demonstrate that HKa is a novel inhibitor of **angiogenesis**, whose activity is dependent on the unique conformation of the two-chain molecule.
ACCESSION NUMBER: 2001111838 MEDLINE
DOCUMENT NUMBER: 20553282 PubMed ID: 11099478
TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and inhibits **angiogenesis**: partial activity within domain 5.
AUTHOR: Zhang J C; Claffey K; Sakthivel R; Darzynkiewicz Z; Shaw D E; Leal J; Wang Y C; Lu F M; McCrae K R
CORPORATE SOURCE: Hematology-Oncology Division, Case Western Reserve University, School of Medicine, Cleveland, Ohio 44106-4937, USA.
CONTRACT NUMBER: CA83134 (NCI)
HL50827 (NHLBI)
SOURCE: FASEB JOURNAL, (2000 Dec) 14 (15) 2589-600.
Journal code: FAS. ISSN: 0892-6638.
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LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20010205
Entered Medline: 20010208

L5 ANSWER 2 OF 19 MEDLINE
TI Domain 5 of high molecular weight **kininogen** (kininostatin)

down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**.

AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would inhibit **angiogenesis**. We found that recombinant domain 5 (D5) inhibited endothelial cell migration toward vitronectin 85% at 0.27 microM with an IC(50) (concentration to yield 50% **inhibition**) = 0.12 microM. A D5 **peptide**, G486-K502, showed an IC(50) = 0.2 microM, but a 25-mer **peptide** from a D3 cell binding domain only inhibited migration 10% at 139 microM (IC(50) > 50 microM). D6 exhibited weaker inhibitory activity (IC(50) = 0.50 microM). D5 also potently inhibited endothelial cell proliferation with an IC(50) = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. **Peptide** 440-455 was the most potent (IC(50) = 100 nM) in inhibiting proliferation but did not inhibit migration. D5 inhibited **angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and **peptide** 400-455 was also inhibitory (79%). HK D5 (for which we suggest the designation, "kininostatin") is a potent inhibitor of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo. (Blood. 2000;95:543-550)

ACCESSION NUMBER: 2000094677 MEDLINE
DOCUMENT NUMBER: 20094677 PubMed ID: 10627460
TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**.
AUTHOR: Colman R W; Jameson B A; Lin Y; Johnson D; Mousa S A
CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA 19140, USA.. colmanr@astro.temple.edu
CONTRACT NUMBER: PO1HL56914 (NHLBI)
RO1CA63938 (NCI)
SOURCE: BLOOD, (2000 Jan 15) 95 (2) 543-50.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000209
Last Updated on STN: 20000209
Entered Medline: 20000203

L5 ANSWER 3 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS

TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**.

AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would inhibit **angiogenesis**. We found that recombinant domain 5 (D5) inhibited endothelial cell migration toward vitronectin 85% at 0.27 muM with an IC50

(concentration to yield 50% **inhibition**) = 0.12 muM. A D5 **peptide**, G486-K502, showed an IC50 = 0.2 muM, but a 25-mer **peptide** from a D[redacted]ell binding domain only inhibi[redacted] migration 10% at 139 muM (IC50 > 50 muM). D6 exhibited weaker inhibitory activity (IC50 = 0.50 muM). D5 also potently inhibited endothelial cell proliferation with an IC50 = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. **Peptide** 440-455 was the most potent (IC50 = 100 nM) in inhibiting proliferation but did not inhibit migration. D5 inhibited **angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and **peptide** 400-455 was also inhibitory (79%). HK D5 (for which we suggest the designation, "kininostatin") is a potent inhibitor of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo.

ACCESSION NUMBER: 2000:104334 BIOSIS
DOCUMENT NUMBER: PREV200000104334
TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**.
AUTHOR(S): Colman, Robert W. (1); Jameson, Bradford A.; Lin, Yingzhang; Johnson, Donald; Mousa, Shaker A.
CORPORATE SOURCE: (1) Temple University School of Medicine, 3400 North Broad St, Philadelphia, PA, 19140 USA
SOURCE: Blood, (Jan. 15, 2000) Vol. 95, No. 2, pp. 543-550. ISSN: 0006-4971.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

L5 ANSWER 4 OF 19 USPATFULL
TI DNA fragmentation factor involved in apoptosis
AB The invention provides methods and compositions relating to DNA Fragmentation Factor (DFF) polypeptides and related nucleic acids. More particularly, the present invention provides the sequence for the active subunit of DFF. The polylpeptides may be produced recombinantly from host cells transformed from the disclosed DFF encoding nucleic acids or purified from human cells. The invention provides isolated DFF hybridization probes and primers capable of specifically hybridization with the disclosed DFF genes, DFF-specific binding agents such as specific antibodies, and methods of making and using the subject compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2000:174366 USPATFULL
TITLE: DNA fragmentation factor involved in apoptosis
INVENTOR(S): Wang, Xiaodong, Dallas, TX, United States
Liu, Xuesong, Dallas, TX, United States
PATENT ASSIGNEE(S): The University of Texas System Board of Regents, Austin, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6165737		20001226	
APPLICATION INFO.:	US 1998-61702		19980416	(9)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Achutamurthy, Ponnathapu
ASSISTANT EXAMINER: Moore, William W.
LEGAL REPRESENTATIVE: Fulbright & Jaworski L.L.P.
NUMBER OF CLAIMS: 20

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 5176
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 5 OF 19 USPATFULL
TI Serine protease inhibitors comprising .alpha.-keto heterocycles
AB Provided are methods of inhibiting the activity of a serine protease using protease inhibitors that include an alpha-keto heterocycle in their structure. The methods are useful in the treatment of ischemic heart or treatment of symptoms associated with blood coagulation disorders. Also provided are methods for detecting or quantifying the activity of a serine protease in a pure sample.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2000:167985 USPATFULL
TITLE: Serine protease inhibitors comprising .alpha.-keto heterocycles
INVENTOR(S): Gyorkos, Albert C., Westminster, CO, United States
Spruce, Lyle W., Arvada, CO, United States
Leimer, Axel H., Lakewood, CO, United States
Cheronis, John C., Conifer, CO, United States
PATENT ASSIGNEE(S): Cortech, Inc., United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6159938		20001212
APPLICATION INFO.:	US 1997-859242		19970520 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1996-761190, filed on 6 Dec 1996, now patented, Pat. No. US 5807829 which is a continuation-in-part of Ser. No. US 1994-345820, filed on 21 Nov 1994, now patented, Pat. No. US 5618792
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Russel, Jeffrey E.
LEGAL REPRESENTATIVE: Dechert
NUMBER OF CLAIMS: 77
EXEMPLARY CLAIM: 1
LINE COUNT: 1841
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 6 OF 19 USPATFULL
TI Method for assaying for modulators of cytokines of the TFG .beta. superfamily
AB The invention relates to a method for assaying for the presence of a substance that modulates a cytokine of the TGF.beta. superfamily. A substance which is suspected of modulating a cytokine of the TGF.beta. superfamily and a TGF.beta. binding compound which is not a TGF.beta. receptor and which contains a TRH1 domain, or a portion or mimetic thereof, is reacted with a cytokine of the TGF.beta. superfamily under conditions where the compound, portion or mimetic thereof, and the cytokine are capable of forming a complex. Complexes, free compound and/or cytokine are assayed and compared with a control. The invention also relates to a composition comprising at least one compound which is not a TGF.beta. receptor and which contains the TRH1 domain or a portion, or a mimetic thereof, and a pharmaceutically acceptable carrier, auxiliary or excipient and to methods of treatment using the composition. Further the invention relates to a method of enhancing the activity of growth factors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 1998:134826 USPATFULL
TITLE: Method for assaying for modulators of cytokines of the TFG .beta. superfamily

INVENTOR(S): Dennis, James W., Etobicoke, Canada
Demetriou, Michael, Toronto, Canada
PATENT ASSIGNEE(S): Mount Sinai Hospital Corporation, Toronto, Canada
(non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5830671		19981103
APPLICATION INFO.:	US 1997-854768		19970512 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1994-237715, filed on 4 May
1994
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Ulm, John
ASSISTANT EXAMINER: Mertz, Prema
LEGAL REPRESENTATIVE: Merchant, Gould, Smith, Edell, Welter & Schmidt
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 1480
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 7 OF 19 USPATFULL
TI Aptamers specific for biomolecules and methods of making
AB A method for identifying oligomer sequences, optionally comprising modified base, which specifically bind target molecules such as serum proteins, kinins, eicosanoids and extracellular proteins is described. The method is used to generate aptamers that bind to serum Factor X, PDGF, FGF, ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface molecules. The technique involves complexation of the target molecule with a mixture of oligonucleotides containing random sequences and sequences which serve as primer for PCR under conditions wherein a complex is formed with the specifically binding sequences, but not with the other members of the oligonucleotide mixture. The complex is then separated from uncomplexed oligonucleotides and the complexed members of the oligonucleotide mixture are recovered from the separated complex using the polymerase chain reaction. The recovered oligonucleotides may be sequenced, and successive rounds of selection using complexation, separation, amplification and recovery can be employed. The oligonucleotides can be used for therapeutic and diagnostic purposes and for generating secondary aptamers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 1998:57716 USPATFULL
TITLE: Aptamers specific for biomolecules and methods of making
INVENTOR(S): Griffin, Linda, Atherton, CA, United States
Albrecht, Glenn, Redwood City, CA, United States
Latham, John, Palo Alto, CA, United States
Leung, Lawrence, Hillsborough, CA, United States
Vermaas, Eric, Oakland, CA, United States
Toole, John J., Burlingame, CA, United States
PATENT ASSIGNEE(S): Gilead Sciences, Inc., Foster City, CA, United States
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5756291		19980526
APPLICATION INFO.:	US 1995-484192		19950607 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1992-934387, filed on 21 Aug 1992, now abandoned
DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Zitomer, Stephanie W.
LEGAL REPRESENTATIVE: Bosse, Mark L.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 8242
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2001 ACS
TI **Inhibition** of **angiogenesis** by high-molecular-weight **kininogen** domain 3 **peptide** analogs
AB **Peptide** analogs the high-mol.-wt. **kininogen** domain 3 are potent inhibitors of **angiogenesis**. The peptides have the formula (a) X1-Asn-Asn-Ala-Thr-Phe-Tyr-Phe-Lys-X2, (b) X3-Cys-Val-Gly-Cys-X4, (c) X5-Leu-Asp-X7-Asn-Ala-Glu-Val-Tyr-X6, or (d) Tyr-Phe-Ile-Asp-Phe-Val-Ala-Arg-Glu-Thr-Thr-X7-Ser-Lys-Glu-Ser (X1-X6 = 0-12 amino acids, more preferably 0-6 amino acids; X7 = Ala, Cys). The peptides may also comprise biol. active fragments of high-mol.-wt. **kininogen** domain 3. Methods of inhibiting endothelial cell proliferation and **angiogenesis** are provided.
ACCESSION NUMBER: 2000:420922 HCAPLUS
DOCUMENT NUMBER: 133:68945
TITLE: **Inhibition** of **angiogenesis** by high-molecular-weight **kininogen** domain 3 **peptide** analogs
INVENTOR(S): McCrae, R. Keith
PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of Higher Education, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035407	A2	20000622	WO 1999-US28465	19991202
WO 2000035407	A3	20000908		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000017494	A1	20000703	AU 2000-17494	19991202

PRIORITY APPLN. INFO.: US 1998-112427 P 19981216
WO 1999-US28465 W 19991202
OTHER SOURCE(S): MARPAT 133:68945

L5 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2001 ACS
TI **Inhibition** of **angiogenesis** and endothelial cell proliferation by high-molecular-weight **kininogen** and **peptide** analogs thereof
AB Two-chain high-mol.-wt. **kininogen**, and **peptide** analogs thereof having homol. to sites within **kininogen** domain 5, are potent inhibitors of **angiogenesis**. The peptides have the formula X1-His-Lys-X-Lys-X2 (X = any amino acid; X1, X2= 0-12 amino acids, more preferably 0-6 amino acids, most preferably 0-3 amino acids). X is preferably an amino acid having a nonpolar side chain, or a polar side

chain which is uncharged at pH 6.0 to 7.0. X is most preferably Asn, Phe or His. Methods of inhibiting endothelial cell proliferation and **angiogenesis** are provided.

ACCESSION NUMBER: 2000:335430 HCAPLUS
DOCUMENT NUMBER: 133:802
TITLE: **Inhibition** of **angiogenesis** and endothelial cell proliferation by high-molecular-weight **kininogen** and **peptide** analogs thereof
INVENTOR(S): Mccrae, R. Keith
PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of Higher Education, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027866	A1	20000518	WO 1999-US26419	19991105

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-107833 P 19981110
OTHER SOURCE(S): MARPAT 133:802
REFERENCE COUNT: 10
REFERENCE(S):
(1) Dennis; US 5830671 A 1998 HCAPLUS
(2) Griffin; US 5756291 A 1998 HCAPLUS
(3) Guerinot; US 5846821 A 1998 HCAPLUS
(4) Heitsch; US 5786365 A 1998 HCAPLUS
(7) Lottspeich; European Journal of Biochemistry 1985, V152, P307 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2001 ACS
TI **Inhibition** of **angiogenesis** by **peptide** analogs of high-molecular-weight **kininogen** domain 5
AB A method for **inhibition** of endothelial cell proliferation in a mammal comprises peptides and proteins of high-mol.-wt. **kininogen** light chain (domain 5). For example, glutathione-S-transferase (GST) fusion proteins with high-mol.-wt. **kininogen** light chain peptides, i.e. Lys(420)-Ser(513) (SEQ ID NO: 10) and His(441)-Ser(626) (SEQ ID NO: 8), at concns. of 0.27 and 0.39 .mu.M, resp. induced 100% **inhibition** of proliferation of human umbilical vein endothelial cells (HUVEC). Also, GST-SEQ ID NO: 10 at a concn. of 0.27 .mu.M achieved 100% **inhibition** of HUVEC migration to vitronectin.

ACCESSION NUMBER: 2000:335256 HCAPLUS
DOCUMENT NUMBER: 132:343359
TITLE: **Inhibition** of **angiogenesis** by **peptide** analogs of high-molecular-weight **kininogen** domain 5
INVENTOR(S): Colman, W. Robert; Mousa, A. Shaker
PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of Higher Education, USA; Dupont Pharmaceuticals Company

SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027415	A2	20000518	WO 1999-US26377	19991109
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1044012	A1	20001018	EP 1999-957529	19991109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-107844 P 19981110
WO 1999-US26377 W 19991109

L5 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2001 ACS
TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**
AB We have demonstrated that high mol. wt. **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-assocd. fibrinolysis. We postulated that HK cell binding domains would inhibit **angiogenesis**. We found that recombinant domain 5 (D5) inhibited endothelial cell migration toward vitronectin 85% at 0.27 .mu.M with an IC50 (concn. to yield 50% **inhibition**) = 0.12 .mu.M. A D5 **peptide**, G486-K502, showed an IC50 = 0.2 .mu.M, but a 25-mer **peptide** from a D3 cell binding domain only inhibited migration 10% at 139 .mu.M (IC50 > 50 .mu.M). D6 exhibited weaker inhibitory activity (IC50 = 0.50 .mu.M). D5 also potently inhibited endothelial cell proliferation with an IC50 = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a mol. homol. model of D5 and designed a series of peptides displaying surface loops. **Peptide** 440-455 was the most potent (IC50 = 100 nM) in inhibiting proliferation but did not inhibit migration. D5 inhibited **angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and **peptide** 400-455 was also inhibitory (79%). HK D5 (for which we suggest the designation, "kininostatin") is a potent inhibitor of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo.
ACCESSION NUMBER: 2000:55516 HCAPLUS
DOCUMENT NUMBER: 132:164060
TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**
AUTHOR(S): Colman, Robert W.; Jameson, Bradford A.; Lin, Yingzhang; Johnson, Donald; Mousa, Shaker A.
CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple

University School of Medicine, Philadelphia, PA, USA
SOURCE: Blood (2000), 95(2), 543-550
CODEN: BLOOAW; ISSN: 0006-497[redacted]
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 52
REFERENCE(S): (1) Asakura, S; J Cell Biol 1992, V116, P465 HCAPLUS
(3) Bacharach, E; Proc Natl Acad Sci U S A 1992, V89, P10686 HCAPLUS
(4) Barnathan, E; Blood 1990, V76, P1795 HCAPLUS
(5) Behrendt, N; J Biol Chem 1991, V266, P7842 HCAPLUS
(7) Bradford, H; Blood 1997, V90, P1508 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 19 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 **peptide** derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 **peptide** inhibits endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case Tyr299-Ser314, and in which native cysteine residues may be replaced by alanine residues. The peptides inhibit endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for inhibiting **angiogenesis**, inhibiting endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present **peptide** was 28 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.
ACCESSION NUMBER: AAY95423 Peptide DGENE
TITLE: Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L5 ANSWER 13 OF 19 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 **peptide** derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 **peptide** inhibits endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in

the HK domain 3, in this case amino acid residues Leu331-Tyr338, and in which native cysteine residues may be replaced by alanine residues. The peptides inhibit endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for inhibiting **angiogenesis**, inhibiting endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present **peptide** was 44 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.

ACCESSION NUMBER: AAY95421 Peptide DGENE
TITLE: Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L5 ANSWER 14 OF 19 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 **peptide** derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 **peptide** inhibits endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Leu331-Tyr338, and in which native cysteine residues may be replaced by alanine residues. The peptides inhibit endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for inhibiting **angiogenesis**, inhibiting endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present **peptide** was 42 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.

ACCESSION NUMBER: AAY95420 Peptide DGENE
TITLE: Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L5 ANSWER 15 OF 19 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 **peptide** derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 **peptide** inhibits endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Cys246-Cys249. The peptides inhibit endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for inhibiting **angiogenesis**, inhibiting endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present **peptide** was 30 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.
ACCESSION NUMBER: AAY95415 Peptide DGENE
TITLE: Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L5 ANSWER 16 OF 19 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 **peptide** derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 **peptide** inhibits endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Asn275-Lys282. The peptides inhibit endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for inhibiting **angiogenesis**, inhibiting endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present **peptide** was less than 0.8 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.
ACCESSION NUMBER: AAY95410 Peptide DGENE
TITLE: Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.

(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L5 ANSWER 17 OF 19 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 **peptide** derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 **peptide** inhibits endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Asn275-Lys282. The peptides inhibit endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for inhibiting **angiogenesis**, inhibiting endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present **peptide** was less than 0.8 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.
ACCESSION NUMBER: AAY95409 Peptide DGENE
TITLE: Composition for inhibiting **angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L5 ANSWER 18 OF 19 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**.
AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would inhibit **angiogenesis**. We found that recombinant domain 5 (D5) inhibited endothelial cell migration toward vitronectin 85% at 0.27 .mu.M with an IC50 (concentration to yield 50% **inhibition**) =0.12 .mu.M. A D5 **peptide**, G486-K502, showed an IC50 = 0.2 .mu.M, but a 25-mer **peptide** from a D3 cell binding domain only inhibited migration 10% at 139 .mu.M (IC50 > 50 .mu.M). D6 exhibited weaker inhibitory activity (IC50 = 0.50 .mu.M). D5 also potently inhibited endothelial cell proliferation with an IC50 = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity

to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. **Peptide** 4[redacted]455 was the most potent (IC50 [redacted]00 nM) In inhibiting proliferation but did not inhibit migration. D5 inhibited **angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and **peptide** 400-455 was also inhibitory (79%). HK D5 (for which we suggest the designation, 'kininostatin') is a potent inhibitor of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo.

ACCESSION NUMBER: 2000028682 EMBASE
TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down- regulates endothelial cell proliferation and migration and inhibits **angiogenesis**.
AUTHOR: Colman R.W.; Jameson B.A.; Lin Y.; Johnson D.; Mousa S.A.
CORPORATE SOURCE: R.W. Colman, Sol Sherry Thrombosis Res. Center, Temple University School of Medicine, 3400 North Broad St, Philadelphia, PA 19140, United States. colmanr@astro.temple.edu
SOURCE: Blood, (15 Jan 2000) 95/2 (543-550).
Refs: 52
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L5 ANSWER 19 OF 19 SCISEARCH COPYRIGHT 2001 ISI (R)
TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and inhibits **angiogenesis**
AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding,domains would inhibit **angiogenesis**. We found that recombinant domain 5 (D5) inhibited endothelial cell migration toward vitronectin 85% at 0.27 mu M with an IC50 (concentration to yield 50% **inhibition**) = 0.12 mu M A D5 **peptide**, G486-K502, showed an IC50 = 0.2 mu M, but a 25-mer **peptide** from a D3 cell binding domain only inhibited migration 10% at 139 mu M (IC50 > 50 mu M). D6 exhibited weaker inhibitory activity (IC50 = 0.50 mu M) D5 also potently inhibited endothelial cell proliferation with an IC50 = 30 nM, while D3 and D6 were inactive, Using deletion mutants of D5, we localized the smallest region for full activity
to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. **Peptide** 440-155 was the most potent (IC50 = 100 nM) in inhibiting proliferation but did not inhibit migration. D5 inhibited **angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and **peptide** 400-455 was also inhibitory (79%), HK D5 (for which we suggest the designation, ''kininostatin'') is a potent inhibitor of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo. (Blood, 2000;95:543-550) (C) 2000 by The American Society of Hematology.
ACCESSION NUMBER: 2000:48248 SCISEARCH
THE GENUINE ARTICLE: 272QG
TITLE: Domain 5 of high molecular weight **kininogen**

(kininostatin) down-regulates endothelial cell proliferation and migration and inhibits an[redacted]genesis

AUTHOR: Colman R W (Reprint); Jameson B A; Lin Y Z; Johnson D; Mousa S A

CORPORATE SOURCE: TEMPLE UNIV, SOL SHERRY THROMBOSIS RES CTR, SCH MED, 3400 N BROAD ST, PHILADELPHIA, PA 19140 (Reprint); MCP HAHNEMANN MED SCH, CTR NEUROVIROL, PHILADELPHIA, PA; DUPONT MERCK PHARMACEUT CO, DIV CARDIOVASC, WILMINGTON, DE 19880

COUNTRY OF AUTHOR: USA

SOURCE: BLOOD, (15 JAN 2000) Vol. 95, No. 2, pp. 543-550. Publisher: AMER SOC HEMATOLOGY, 1200 19TH ST, NW, STE 300, WASHINGTON, DC 20036-2422. ISSN: 0006-4971.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE; CLIN

LANGUAGE: English

REFERENCE COUNT: 51

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

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(FILE 'HOME' ENTERED AT 13:14:38 ON 13 JUL 2001)

FILE 'MEDLINE, BIOSIS, USPATFULL, HCAPLUS, DGENE, EMBASE, SCISEARCH, WPIDS, JAPIO, JICST-EPLUS, FSTA, FROSTI, CEN, CEABA-VTB, CABA' ENTERED AT 13:15:24 ON 13 JUL 2001

L1 111516 S ANGIOGENESIS
L2 20392 S L1 AND INHIBITION
L3 6317 S L2 AND PEPTIDE
L4 10807 S KININOGEN
L5 19 S L3 AND L4

=> e MCCRAE, k/au

E1 6 MCCRAE WILLIAM/AU
E2 2 MCCRAE WM/AU
E3 0 --> MCCRAE, K/AU
E4 1 MCCRAEHOMSMA C H/AU
E5 1 MCCRAEKEN G M/AU
E6 1 MCCRAEY E/AU
E7 1 MCCRAIG A/AU
E8 1 MCCRAIG C D/AU
E9 1 MCCRAIG D J/AU
E10 1 MCCRAIG J/AU
E11 1 MCCRAIG J OSCAR/AU
E12 1 MCCRAIG L F/AU

=> e colman,r/au

E1 1 COLMAN WM P/AU
E2 2 COLMAN Y/AU
E3 0 --> COLMAN,R/AU
E4 2 COLMANDEJEAN T/AU
E5 1 COLMANET G/AU
E6 4 COLMANET S/AU
E7 32 COLMANET S F/AU
E8 3 COLMANET SILVANO/AU

E9 1 COLMANET SILVANO E/AU
E10 25 COLMANET SILVANO F/AU
E11 5 CO[redacted]NETTI A L/AU
E12 2 COLMANLERNER A/AU

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(FILE 'HOME' ENTERED AT 13:14:38 ON 13 JUL 2001)

FILE 'MEDLINE, BIOSIS, USPATFULL, HCAPLUS, DGENE, EMBASE, SCISEARCH, WPIDS, JAPIO, JICST-EPLUS, FSTA, FROSTI, CEN, CEABA-VTB, CABA' ENTERED AT
13:15:24 ON 13 JUL 2001
L1 111516 S ANGIOGENESIS
L2 20392 S L1 AND INHIBITION
L3 6317 S L2 AND PEPTIDE
L4 10807 S KININOGEN
L5 19 S L3 AND L4
E MCCRAE, K/AU
E COLMAN,R/AU

=> s l4 ans l1

MISSING OPERATOR L4 ANS
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l4 and l1

L6 107 L4 AND L1

=> s l6 and inhibit?

13 FILES SEARCHED...
L7 95 L6 AND INHIBIT?

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L7 ANSWER 1 OF 95 MEDLINE
TI Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: partial activity within domain 5.
AB We previously reported that the binding of two-chain high molecular weight **kininogen** (HKa) to endothelial cells may occur through interactions with endothelial urokinase receptors. Since the binding of urokinase to urokinase receptors activates signaling responses and may stimulate mitogenesis, we assessed the effect of HKa binding on endothelial cell proliferation. Unexpectedly, HKa **inhibited** proliferation in response to several growth factors, with 50% **inhibition** caused by approximately 10 nM HKa. This activity was Zn(2+) dependent and not shared by either single-chain high molecular weight **kininogen** (HK) or low molecular weight **kininogen** . HKa selectively **inhibited** the proliferation of human umbilical vein and dermal microvascular endothelial cells, but did not affect that of umbilical vein or human aortic smooth muscle cells, trophoblasts, fibroblasts, or carcinoma cells. **Inhibition** of endothelial proliferation by HKa was associated with endothelial cell apoptosis and unaffected by antibodies that block the binding of HK or HKa to any of their known endothelial receptors. Recombinant HK domain 5 displayed activity similar to that of HKa. In vivo, HKa **inhibited** neovascularization of subcutaneously implanted Matrigel plugs, as well as

rat corneal **angiogenesis**. These results demonstrate that HKa is a novel **inhibitor** of **angiogenesis**, whose activity is dependent on the unique conformation of the two-chain molecule.

ACCESSION NUMBER: 2001111838 MEDLINE
DOCUMENT NUMBER: 20553282 PubMed ID: 11099478
TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits** **angiogenesis**: partial activity within domain 5.
AUTHOR: Zhang J C; Claffey K; Sakthivel R; Darzynkiewicz Z; Shaw D E; Leal J; Wang Y C; Lu F M; McCrae K R
CORPORATE SOURCE: Hematology-Oncology Division, Case Western Reserve University, School of Medicine, Cleveland, Ohio 44106-4937, USA.
CONTRACT NUMBER: CA83134 (NCI)
HL50827 (NHLBI)
SOURCE: FASEB JOURNAL, (2000 Dec) 14 (15) 2589-600.
Journal code: FAS. ISSN: 0892-6638.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20010205
Entered Medline: 20010208

L7 ANSWER 2 OF 95 MEDLINE
TI Local delivery of human tissue kallikrein gene accelerates spontaneous **angiogenesis** in mouse model of hindlimb ischemia.
AB BACKGROUND: Human tissue kallikrein (HK) releases kinins from **kininogen**. We investigated whether adenovirus-mediated HK gene delivery is angiogenic in the context of ischemia. METHODS AND RESULTS: Hindlimb ischemia, caused by femoral artery excision, increased muscular capillary density (P:<0.001) and induced the expression of kinin B(1) receptor gene (P:<0.05). Pharmacological blockade of B(1) receptors blunted ischemia-induced **angiogenesis** (P:<0.01), whereas kinin B(2) receptor antagonism was ineffective. Intramuscular delivery of adenovirus containing the HK gene (Ad. CMV-cHK) enhanced the increase in capillary density caused by ischemia (969+/-32 versus 541+/-18 capillaries/mm(2) for control, P:<0.001), accelerated blood flow recovery (P:<0.01), and preserved energetic charge of ischemic muscle (P:<0.01). Chronic blockade of kinin B(1) or B(2) receptors prevented HK-induced **angiogenesis**. CONCLUSIONS: HK gene delivery enhances the native angiogenic response to ischemia. **Angiogenesis** gene therapy with HK might be applicable to peripheral occlusive vascular disease.

ACCESSION NUMBER: 2001087991 MEDLINE
DOCUMENT NUMBER: 20579827 PubMed ID: 11136697
TITLE: Local delivery of human tissue kallikrein gene accelerates spontaneous **angiogenesis** in mouse model of hindlimb ischemia.
AUTHOR: Emanueli C; Minasi A; Zacheo A; Chao J; Chao L; Salis M B; Straino S; Tozzi M G; Smith R; Gaspa L; Bianchini G; Stillo F; Capogrossi M C; Madeddu P
CORPORATE SOURCE: Laboratorio di Patologia Vascolare, Istituto Dermopatico dell'Immacolata, Rome, Italy.
CONTRACT NUMBER: HL-29397 (NHLBI)
HL-52196 (NHLBI)
SOURCE: CIRCULATION, (2001 Jan 2) 103 (1) 125-32.
Journal code: DAW; 0147763. ISSN: 1524-4539.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 2[redacted]01
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010521
Entered PubMed: 20010109
Entered Medline: 20010118

L7 ANSWER 3 OF 95 MEDLINE
TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis.**
AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would **inhibit angiogenesis.** We found that recombinant domain 5 (D5) **inhibited** endothelial cell migration toward vitronectin 85% at 0.27 microM with an IC(50) (concentration to yield 50% **inhibition**) = 0.12 microM. A D5 peptide, G486-K502, showed an IC(50) = 0.2 microM, but a 25-mer peptide from a D3 cell binding domain only **inhibited** migration 10% at 139 microM (IC(50) > 50 microM). D6 exhibited weaker **inhibitory** activity (IC(50) = 0.50 microM). D5 also potently **inhibited** endothelial cell proliferation with an IC(50) = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. Peptide 440-455 was the most potent (IC(50) = 100 nM) in **inhibiting** proliferation but did not **inhibit** migration. D5 **inhibited angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and peptide 400-455 was also **inhibitory** (79%). HK D5 (for which we suggest the designation, "kininostatin") is a potent **inhibitor** of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo. (Blood. 2000;95:543-550)
ACCESSION NUMBER: 2000094677 MEDLINE
DOCUMENT NUMBER: 20094677 PubMed ID: 10627460
TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis.**
AUTHOR: Colman R W; Jameson B A; Lin Y; Johnson D; Mousa S A
CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA 19140, USA..
colmanr@astro.temple.edu
CONTRACT NUMBER: PO1HL56914 (NHLBI)
RO1CA63938 (NCI)
SOURCE: BLOOD, (2000 Jan 15) 95 (2) 543-50.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000209
Last Updated on STN: 20000209
Entered Medline: 20000203

L7 ANSWER 4 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS

TI Peptides derived from high molecular weight **kininogen** (HK) domains 3 and 5 **inhibit** endothelial cell proliferation and induce endothelial cell apoptosis.

AB We have recently reported that two-chain high molecular weight **kininogen** (HKa) **inhibits** endothelial cell proliferation, induces endothelial cell apoptosis and **inhibits** **angiogenesis**. Recombinant high molecular weight **kininogen** domain 5 expresses similar activity, **inhibiting** endothelial cell proliferation by 50% (IC50) at a concentration of apprx60 nM. To further define the regions within **kininogen** domain 5 responsible for these effects, we prepared overlapping 16 amino acid peptides (each overlapping by 8 amino acids) encompassing **kininogen** domain 5 (aa 384-509), and measured their ability to **inhibit** endothelial cell proliferation and induce endothelial cell apoptosis. A similar strategy was used to assess potentially active regions within HK domain 3, which also contains regions that mediate binding of HK to endothelial cells. The most potent domain 5-derived peptides were found in the C-terminal region of the domain. H5-13 (KHGHGHGKHKNKGKKN; aa 480-495 of HK) **inhibited** endothelial cell proliferation by 86 +- 13% at a concentration of 50 muM (IC50 apprx 8 muM), while H5-14 (HKNKGKKNGKHNGWKT; aa 488-503 of HK), used at the same concentration, **inhibited** proliferation by 93 +- 7% (IC50 apprx 14 muM). As observed with HKa and recombinant domain 5, the peptides caused endothelial cell apoptosis, and their activity was enhanced in the presence of Zn2+. These results differ from a previous report, in which the domain 5 peptide most active in **inhibiting** endothelial cell proliferation was found to encompass amino acids 440-455 of HK. In addition, we also observed that two 16 amino acid peptides from HK domain 3 (H3-6, aa 267-282 of HK; H3-7, aa 275-290 of HK) also **inhibited** endothelial cell proliferation (IC50 apprx 1 muM) and induced apoptosis, though they were not freely soluble in aqueous buffers. Exogenous Zn2+ did not significantly affect the activity of the latter peptides. Neither the domain 3 or domain 5 peptides affected the proliferation of a number of other cell types, including primary cultures of fibroblasts and smooth muscle cells. These studies define active regions within HK domains 3 and 5 that **inhibit** endothelial cell proliferation and induce endothelial cell apoptosis. Current studies are focused on evaluating the antiangiogenic activity of these peptides in vitro.

ACCESSION NUMBER: 2001:312300 BIOSIS

DOCUMENT NUMBER: PREV200100312300

TITLE: Peptides derived from high molecular weight **kininogen** (HK) domains 3 and 5 **inhibit** endothelial cell proliferation and induce endothelial cell apoptosis.

AUTHOR(S): Zhang, Jing-Chuan (1); Juarez, Jose; Shaw, David Elliott; Mazar, Andrew P.; McCrae, Keith R. (1)

CORPORATE SOURCE: (1) Hematology-Oncology, Case Western Reserve University School of Medicine, Cleveland, OH USA

SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 41a.
print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

L7 ANSWER 5 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI Kininostatin induces apoptosis of endothelial cells.
AB Kininostatin (D5) domain 5 of high molecular weight **kininogen** (HK), is a recently discovered angiogenic **inhibitor**. Previously we reported that D5 **inhibited** two important steps required for **angiogenesis**: proliferation and migration of endothelial cells. Anti-angiogenic activity was further demonstrated in an in vivo model by studying neovascularization in the CAM (Chicken chorioAllantoic Membrane).

D5 **inhibited** new blood vessel formation 85% compared to that stimulated by bFGF in CAM. We proposed that D5 may functions as a naturally occurring **angiogenesis inhibitor** because it is proteolytically cleaved from HK, a multifunctional plasma protein that plays important roles in adhesion, fibrinolysis and inflammation. To understand the mechanism of the antiangiogenic effect of D5, we investigated whether the **inhibition** of endothelial cell proliferation is associated with induction of apoptosis. We found that human umbilical vein endothelial cells (HUVEC) undergo rapid apoptosis when cultured in a serum-free medium, and this alteration can be prevented by addition of 10 ng/ml bFGF. Recombinant D5 (200 nM) attenuated the protective effect of bFGF by 80%. The cells treated with D5 in the presence of bFGF showed typical morphological features of apoptosis, such as membrane blebbing and shrinkage of the cell body. The apoptotic cell death was further confirmed by two additional assays: Hoechst 33258 cell staining and DNA fragmentation analysis. D5-treated cells in the presence of bFGF showed an increased number of apoptotic nuclei and an increased amount of fragmented DNA. An interesting finding of this study is that the number of apoptotic cells was significantly higher among the proliferating cells than among quiescent cells as determined by a microscopic analysis simultaneously detecting mitotic and apoptotic cells. We conclude that D5-induced apoptosis, particularly among proliferating endothelial cells, makes an important contribution to its anti-angiogenic activity.

ACCESSION NUMBER: 2001:264349 BIOSIS
DOCUMENT NUMBER: PREV200100264349
TITLE: Kininostatin induces apoptosis of endothelial cells.
AUTHOR(S): Colman, Robert W. (1); Wang, Shujie (1); Guo, Yan-Lin (1)
CORPORATE SOURCE: (1) Thrombosis Res. Ctr., Temple Univ. Sch. of Med., 3400 N. Broad Street, Philadelphia, PA, 19140 USA
SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A459. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 6 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**.
AB Cleavage of high molecular weight **kininogen** (HK) by plasma kallikrein results in a light chain and a heavy chain (HK). The light chain has two domains: D6, which binds (pre)kallikrein, and D5, which binds to anionic surfaces, including heparin as well as zinc. Initially, HK was thought to be important for surface-activated coagulation. HKa or D5 binds to the urokinase receptor on endothelial cells, thereby enhancing the conversion of prourokinase to urokinase by kallikrein, and, thus, cell-associated fibrinolysis. HKa or D5 is antiadhesive by competing with

vitronectin binding to the urokinase receptor and/or forming a complex with vitronectin. D5 **inhibits** endothelial cell migration, proliferation, t[redacted] formation and **angiogenesis**, t[redacted] modulating inflammation and neovascularization.

ACCESSION NUMBER: 2001:207350 BIOSIS
DOCUMENT NUMBER: PREV200100207350
TITLE: Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**.
AUTHOR(S): Colman, Robert W. (1)
CORPORATE SOURCE: (1) Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA, 19140 USA
SOURCE: Biological Chemistry, (January, 2001) Vol. 382, No. 1, pp. 65-70. print.
ISSN: 1431-6730.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 7 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: Partial activity within domain 5.
AB We previously reported that the binding of two-chain high molecular weight **kininogen** (HKa) to endothelial cells may occur through interactions with endothelial urokinase receptors. Since the binding of urokinase to urokinase receptors activates signaling responses and may stimulate mitogenesis, we assessed the effect of HKa binding on endothelial cell proliferation. Unexpectedly, HKa **inhibited** proliferation in response to several growth factors, with 50% **inhibition** caused by apprx 10 nM HKa. This activity was Zn2+ dependent and not shared by either single-chain high molecular weight **kininogen** (HK) or low molecular weight **kininogen**. HKa selectively **inhibited** the proliferation of human umbilical vein and dermal microvascular endothelial cells, but did not affect that of umbilical vein or human aortic smooth muscle cells, trophoblasts, fibroblasts, or carcinoma cells. **Inhibition** of endothelial proliferation by HKa was associated with endothelial cell apoptosis and unaffected by antibodies that block the binding of HK or HKa to any of their known endothelial receptors. Recombinant HK domain 5 displayed activity similar to that of HKa. In vivo, HKa **inhibited** neovascularization of subcutaneously implanted Matrigel plugs, as well as rat corneal **angiogenesis**. These results demonstrate that HKa is a novel **inhibitor** of antiogenesis, whose activity is dependent on the unique conformation of the two-chain molecule.

ACCESSION NUMBER: 2001:58828 BIOSIS
DOCUMENT NUMBER: PREV200100058828
TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: Partial activity within domain 5.
AUTHOR(S): Zhang, Jing-Chuan; Claffey, Kevin; Sakthivel, Ramasamy; Darzynkiewicz, Zbigniev; Shaw, David Elliot; Leal, Juan; Wang, Yi-Chun; Lu, Feng-Min; Mccrae, Keith R. (1)
CORPORATE SOURCE: (1) Hematology-Oncology Division, Case Western Reserve University, School of Medicine, 10900 Euclid Ave., BRB 3, Cleveland, OH, 44106-4937: kxm71@pocwru.edu USA
SOURCE: FASEB Journal, (December, 2000) Vol. 14, No. 15, pp. 2589-2600. print.
ISSN: 0892-6638.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 8 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI **Inhibition** of **angiogenesis** by peptides derived fr[redacted]
kininogen domain[redacted] and by a monoclonal antibody t[redacted]
kininogen domain 5.
ACCESSION NUMBER: 2000:368311 BIOSIS
DOCUMENT NUMBER: PREV200000368311
TITLE: **Inhibition** of **angiogenesis** by peptides derived from **kininogen** domain 5 and by a monoclonal antibody to **kininogen** domain 5.
AUTHOR(S): Mousa, S. A. (1); Mohamed, S.; Powell, J.; Colman, R. W.
CORPORATE SOURCE: (1) DuPont Pharmaceuticals, Wilmington, DE USA
SOURCE: Fibrinolysis & Proteolysis, (June, 2000) Vol. 14, No. Supplement 1, pp. 39. print.
Meeting Info.: XVth International Congress on Fibrinolysis and Proteolysis Hamamatsu, Japan June 25-29, 2000
ISSN: 1369-0191.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 9 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI **Inhibition** of **angiogenesis** by peptides derived from **kininogen** domain 5 & by a monoclonal antibody to **kininogen** domain 5.
ACCESSION NUMBER: 2000:176604 BIOSIS
DOCUMENT NUMBER: PREV200000176604
TITLE: **Inhibition** of **angiogenesis** by peptides derived from **kininogen** domain 5 & by a monoclonal antibody to **kininogen** domain 5.
AUTHOR(S): Mousa, Shaker A. (1); Mohamed, Seema; Powell, John; Colman,
Robert W.
CORPORATE SOURCE: (1) DuPont Pharmaceuticals, Wilmington, DE USA
SOURCE: Journal of the American College of Cardiology., (Feb., 2000) Vol. 35, No. 2 suppl. A, pp. 295A-296A.
Meeting Info.: 29th Annual Scientific Session of the American College of Cardiology. Anaheim, California, USA March 12-15, 2000
ISSN: 0735-1097.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 10 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.
AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK
cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would **inhibit angiogenesis**. We found that recombinant domain 5 (D5) **inhibited** endothelial cell migration toward vitronectin 85% at 0.27 muM with an IC50 (concentration to yield 50% **inhibition**) = 0.12 muM. A D5 peptide, G486-K502, showed an IC50 = 0.2 muM, but a 25-mer peptide from a D3 cell binding domain only **inhibited** migration 10% at 139 muM (IC50 > 50 muM). D6 exhibited weaker **inhibitory** activity (IC50 = 0.50 muM). D5 also potently **inhibited** endothelial cell proliferation with an IC50 = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the

active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. Peptide 440-455 was the most potent (IC50 = 1[redacted] nM) in **inhibiting** proliferatio[redacted]ut did not **inhibit** migration. D5 **inhibited angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and peptide 400-455 was also **inhibitory** (79%). HK D5 (for which we suggest the designation, "kininostatin") is a potent **inhibitor** of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo.

ACCESSION NUMBER: 2000:104334 BIOSIS
DOCUMENT NUMBER: PREV200000104334
TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.
AUTHOR(S): Colman, Robert W. (1); Jameson, Bradford A.; Lin, Yingzhang; Johnson, Donald; Mousa, Shaker A.
CORPORATE SOURCE: (1) Temple University School of Medicine, 3400 North Broad St, Philadelphia, PA, 19140 USA
SOURCE: Blood, (Jan. 15, 2000) Vol. 95, No. 2, pp. 543-550. ISSN: 0006-4971.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 11 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI Biologic activities of the contact factors in vivo: Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis** and thrombosis.
ACCESSION NUMBER: 2000:87674 BIOSIS
DOCUMENT NUMBER: PREV200000087674
TITLE: Biologic activities of the contact factors in vivo: Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis** and thrombosis.
AUTHOR(S): Colman, Robert W. (1)
CORPORATE SOURCE: (1) Sol Sherry Thrombosis Research Center, Temple University School of Medicine, 3400 North Broad Street, Philadelphia, PA, 19140 USA
SOURCE: Thrombosis and Haemostasis, (Dec., 1999) Vol. 82, No. 6, pp. 1568-1577. ISSN: 0340-6245.
DOCUMENT TYPE: General Review
LANGUAGE: English

L7 ANSWER 12 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI **Inhibition** of **angiogenesis** by two-chain high molecular weight **kininogen** (HKa) is associated with induction of endothelial cell apoptosis.
ACCESSION NUMBER: 2000:46733 BIOSIS
DOCUMENT NUMBER: PREV200000046733
TITLE: **Inhibition** of **angiogenesis** by two-chain high molecular weight **kininogen** (HKa) is associated with induction of endothelial cell apoptosis.
AUTHOR(S): Zhang, Jing-Chuan (1); Sakthivel, Ramasamy (1); Lu, Feng-Min; Darzynkiewicz, Zbigniev; McCrae, Keith R. (1)
CORPORATE SOURCE: (1) Hematology-Oncology, Case Western Reserve University School of Medicine, Cleveland, OH USA
SOURCE: Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp.
11a.
Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December

3-7, 1999 The American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 13 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI **Inhibition** of tumor **angiogenesis** by a monoclonal antibody to **kininogen** domain 5.
ACCESSION NUMBER: 2000:46729 BIOSIS
DOCUMENT NUMBER: PREV200000046729
TITLE: **Inhibition** of tumor **angiogenesis** by a monoclonal antibody to **kininogen** domain 5.
AUTHOR(S): Colman, Robert W. (1); Mousa, Shaker A.
CORPORATE SOURCE: (1) Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA USA
SOURCE: Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp.
10a.
Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999 The American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 14 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI Two chain high molecular weight **kininogen inhibits** endothelial cell proliferation and **angiogenesis**: Partial activity within domain 5.
ACCESSION NUMBER: 2000:42551 BIOSIS
DOCUMENT NUMBER: PREV200000042551
TITLE: Two chain high molecular weight **kininogen inhibits** endothelial cell proliferation and **angiogenesis**: Partial activity within domain 5.
AUTHOR(S): Zhang, Jing-Chuan (1); Claffey, Kevin P.; Sakthivel, Ramasamy (1); Leal, Juan; McCrae, Keith R. (1)
CORPORATE SOURCE: (1) Hematology-Oncology, Case Western Reserve University School of Medicine, Cleveland, OH USA
SOURCE: Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp.
10a.
Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999 The American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 15 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI Domain 5 of high molecular weight **kininogen** (kininostatin) downregulates endothelial cell proliferation and migration and **inhibits angiogenesis**.
ACCESSION NUMBER: 1999:308253 BIOSIS
DOCUMENT NUMBER: PREV199900308253
TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) downregulates endothelial cell proliferation
and migration and **inhibits angiogenesis**
.
AUTHOR(S): Colman, R. W. (1); Jameson, B.; Mousa, S. A.
CORPORATE SOURCE: (1) Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA USA
SOURCE: FASEB Journal, (April 23, 1999) Vol. 13, No. 7, pp. A1407.

Meeting Info.: Annual Meeting of the American Societies for
Experimental Biology on Biochemistry and Molecular Biology 99 San Francisco, California, USA May 16-20, 1999 American Societies for Experimental Biology
. ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 16 OF 95 BIOSIS COPYRIGHT 2001 BIOSIS
TI **Inhibition** of **angiogenesis** by peptides derived from **kininogen.**
ACCESSION NUMBER: 1999:96019 BIOSIS
DOCUMENT NUMBER: PREV199900096019
TITLE: **Inhibition** of **angiogenesis** by peptides derived from **kininogen.**
AUTHOR(S): Colman, R. W. (1); Lin, Y.; Johnson, D.; Mousa, S. A.
CORPORATE SOURCE: (1) Sol Sherry Thrombosis Res. Center, Temple Univ. Sch. Med., Philadelphia, PA USA
SOURCE: Blood, (Nov. 15, 1998) Vol. 92, No. 10 SUPPL. 1 PART 1-2, pp. 174A.
Meeting Info.: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998 The American Society of Heamatology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 17 OF 95 USPATFULL
TI DNA fragmentation factor involved in apoptosis
AB The invention provides methods and compositions relating to DNA Fragmentation Factor (DFF) polypeptides and related nucleic acids. More particularly, the present invention provides the sequence for the active subunit of DFF. The polylpeptides may be produced recombinantly from host cells transformed from the disclosed DFF encoding nucleic acids or purified from human cells. The invention provides isolated DFF hybridization probes and primers capable of specifically hybridization with the disclosed DFF genes, DFF-specific binding agents such as specific antibodies, and methods of making and using the subject compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2000:174366 USPATFULL
TITLE: DNA fragmentation factor involved in apoptosis
INVENTOR(S): Wang, Xiaodong, Dallas, TX, United States
Liu, Xuesong, Dallas, TX, United States
PATENT ASSIGNEE(S): The University of Texas System Board of Regents, Austin, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6165737		20001226	
APPLICATION INFO.:	US 1998-61702		19980416	(9)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Achutamurthy, Ponnathapu
ASSISTANT EXAMINER: Moore, William W.
LEGAL REPRESENTATIVE: Fulbright & Jaworski L.L.P.
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 5176
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 18 OF 95 USPATFULL
TI Serine protease **inhibitors** comprising .alpha.-keto heterocycles
AB Provided are methods of **inhibiting** the activity of a serine protease using protease **inhibitors** that include an alpha-keto heterocycle in their structure. The methods are useful in the treatment of ischemic heart or treatment of symptoms associated with blood coagulation disorders. Also provided are methods for detecting or quantifying the activity of a serine protease in a pure sample.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2000:167985 USPATFULL
TITLE:	Serine protease **inhibitors** comprising .alpha.-keto heterocycles
INVENTOR(S):	Gyorkos, Albert C., Westminster, CO, United States Spruce, Lyle W., Arvada, CO, United States Leimer, Axel H., Lakewood, CO, United States Cheronis, John C., Conifer, CO, United States
PATENT ASSIGNEE(S):	Cortech, Inc., United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6159938		20001212
APPLICATION INFO.:	US 1997-859242		19970520 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1996-761190, filed on 6 Dec 1996, now patented, Pat. No. US 5807829 which is a continuation-in-part of Ser. No. US 1994-345820, filed on 21 Nov 1994, now patented, Pat. No. US 5618792		
DOCUMENT TYPE:	Utility		
PRIMARY EXAMINER:	Russel, Jeffrey E.		
LEGAL REPRESENTATIVE:	Dechert		
NUMBER OF CLAIMS:	77		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1841		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 19 OF 95 USPATFULL
TI Method for assaying for modulators of cytokines of the TFG .beta. superfamily
AB The invention relates to a method for assaying for the presence of a substance that modulates a cytokine of the TGF.beta. superfamily. A substance which is suspected of modulating a cytokine of the TGF.beta. superfamily and a TGF.beta. binding compound which is not a TGF.beta. receptor and which contains a TRH1 domain, or a portion or mimetic thereof, is reacted with a cytokine of the TGF.beta. superfamily under conditions where the compound, portion or mimetic thereof, and the cytokine are capable of forming a complex. Complexes, free compound and/or cytokine are assayed and compared with a control. The invention also relates to a composition comprising at least one compound which is not a TGF.beta. receptor and which contains the TRH1 domain or a portion, or a mimetic thereof, and a pharmaceutically acceptable carrier, auxiliary or excipient and to methods of treatment using the composition. Further the invention relates to a method of enhancing the activity of growth factors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	1998:134826 USPATFULL
TITLE:	Method for assaying for modulators of cytokines of the TFG .beta. superfamily
INVENTOR(S):	Dennis, James W., Etobicoke, Canada Demetriou, Michael, Toronto, Canada
PATENT ASSIGNEE(S):	Mount Sinai Hospital Corporation, Toronto, Canada (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5830671		19981103
APPLICATION INFO.:	US 1997-854768		19970512 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1994-237715, filed on 4 May 1994
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Ulm, John
ASSISTANT EXAMINER: Mertz, Prema
LEGAL REPRESENTATIVE: Merchant, Gould, Smith, Edell, Welter & Schmidt
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 1480
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 20 OF 95 USPATFULL
TI Aptamers specific for biomolecules and methods of making
AB A method for identifying oligomer sequences, optionally comprising modified base, which specifically bind target molecules such as serum proteins, kinins, eicosanoids and extracellular proteins is described. The method is used to generate aptamers that bind to serum Factor X, PDGF, FGF, ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface molecules. The technique involves complexation of the target molecule with a mixture of oligonucleotides containing random sequences and sequences which serve as primer for PCR under conditions wherein a complex is formed with the specifically binding sequences, but not with the other members of the oligonucleotide mixture. The complex is then separated from uncomplexed oligonucleotides and the complexed members of the oligonucleotide mixture are recovered from the separated complex using the polymerase chain reaction. The recovered oligonucleotides may be sequenced, and successive rounds of selection using complexation, separation, amplification and recovery can be employed. The oligonucleotides can be used for therapeutic and diagnostic purposes and for generating secondary aptamers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 1998:57716 USPATFULL
TITLE: Aptamers specific for biomolecules and methods of making
INVENTOR(S): Griffin, Linda, Atherton, CA, United States
Albrecht, Glenn, Redwood City, CA, United States
Latham, John, Palo Alto, CA, United States
Leung, Lawrence, Hillsborough, CA, United States
Vermaas, Eric, Oakland, CA, United States
Toole, John J., Burlingame, CA, United States
PATENT ASSIGNEE(S): Gilead Sciences, Inc., Foster City, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5756291		19980526
APPLICATION INFO.:	US 1995-484192		19950607 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1992-934387, filed on 21 Aug 1992, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Zitomer, Stephanie W.
LEGAL REPRESENTATIVE: Bosse, Mark L.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: [redacted]12
CAS INDEXING IS AVAILABL[redacted]OR THIS PATENT.

L7 ANSWER 21 OF 95 HCAPLUS COPYRIGHT 2001 ACS
TI **Inhibition** of **angiogenesis** by antibodies against high molecular weight **kininogen** domain 5
AB Antibodies directed against an antigenic determinant of high mol. wt. **kininogen** domain 5, particularly a determinant located in the region formed by light chain amino acids Gly(440) to Lys(502), **inhibit angiogenesis.**
ACCESSION NUMBER: 2001:359837 HCAPLUS
DOCUMENT NUMBER: 134:365709
TITLE: **Inhibition** of **angiogenesis** by antibodies against high molecular weight **kininogen** domain 5
INVENTOR(S): Colman, Robert W.; Mousa, Shaker A.
PATENT ASSIGNEE(S): Temple University of the Commonwealth System of Higher Education, USA; DuPont Pharmaceuticals Company
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034195	A1	20010517	WO 2000-US30975	20001110

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165165 P 19991112
REFERENCE COUNT: 7
REFERENCE(S):
(3) Hasan; Jnl Biol Chem 1995, V270(33), P19256 HCAPLUS
(4) Khan; Am J Physiol 1998, V275(1 Pt 2), PH145 MEDLINE
(5) McCrae, R; WO 0027866 2000 HCAPLUS
(6) Reddigari; Blood 1993, V81(5), P1306 HCAPLUS
(7) Shariat-Madar; Trds Cardio Med 1999, V9(8), P238 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 22 OF 95 HCAPLUS COPYRIGHT 2001 ACS
TI Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**
AB A review with 22 refs. Cleavage of high mol. wt. **kininogen** (HK) by plasma kallikrein results in a light chain and a heavy chain (HK). The light chain has two domains: D6, which binds (pre)kallikrein, and D5, which binds to anionic surfaces, including heparin as well as zinc. Initially, HK was thought to be important for surface-activated coagulation. HKa or D5 binds to the urokinase receptor on endothelial cells, thereby enhancing the conversion of prourokinase to urokinase by kallikrein, and, thus, cell-assocd. fibrinolysis. HKa or D5 is antiadhesive by competing with vitronectin binding to the urokinase

receptor and/or forming a complex with vitronectin. D5 **inhibits** endothelial cell migration, proliferation, tube formation and **angiogenesis**, thus modulating inflammation and neovascularization.

ACCESSION NUMBER: 2001:216006 HCAPLUS
DOCUMENT NUMBER: 134:261312
TITLE: Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**
AUTHOR(S): Colman, Robert W.
CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA, 19140, USA
SOURCE: Biol. Chem. (2001), 382(1), 65-70
CODEN: BICHF3; ISSN: 1431-6730
PUBLISHER: Walter de Gruyter GmbH & Co. KG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 22
REFERENCE(S): (1) Chavakis, T; Blood 2000, V96, P514 HCAPLUS
(4) Colman, R; J Clin Invest 1997, V100, P1481 HCAPLUS
(6) Hasan, A; Proc Natl Acad Sci 1998, V95, P3615 HCAPLUS
(7) Herwald, H; J Biol Chem 1996, V271, P13040 HCAPLUS
(9) Ichinose, A; J Biol Chem 1986, V261, P3486 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 95 HCAPLUS COPYRIGHT 2001 ACS
TI Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: partial activity within domain 5
AB We previously reported that the binding of two-chain high mol. wt. **kininogen** (HKa) to endothelial cells may occur through interactions with endothelial urokinase receptors. Since the binding of urokinase to urokinase receptors activates signaling responses and may stimulate mitogenesis, we assessed the effect of HKa binding on endothelial cell proliferation. Unexpectedly, HKa **inhibited** proliferation in response to several growth factors, with 50% **inhibition** caused by .apprx.10 nM HKa. This activity was Zn2+ dependent and not shared by either single-chain high mol. wt. **kininogen** (HK) or low mol. wt. **kininogen**. HKa selectively **inhibited** the proliferation of human umbilical vein and dermal microvascular endothelial cells, but did not affect that of umbilical vein or human aortic smooth muscle cells, trophoblasts, fibroblasts, or carcinoma cells. **Inhibition** of endothelial proliferation by HKa was assocd. with endothelial cell apoptosis and unaffected by antibodies that block the binding of HK or HKa to any of their known endothelial receptors. Recombinant HK domain 5 displayed activity similar to that of HKa. In vivo, HKa **inhibited** neovascularization of s.c. implanted Matrigel plugs, as well as rat corneal **angiogenesis**. These results demonstrate that HKa is a novel **inhibitor** of **angiogenesis**, whose activity is dependent on the unique conformation of the two-chain mol.

ACCESSION NUMBER: 2001:120471 HCAPLUS
DOCUMENT NUMBER: 134:173152
TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: partial activity within domain 5
AUTHOR(S): Zhang, Jing-Chuan; Claffey, Kevin; Sakthivel, Ramasamy; Darzynkiewicz, Zbigniev; Shaw, David Elliot;

Leal, Juan; Wang, Yi-Chun; Lu, Feng-Min; Mccrae, Keith

CORPORATE SOURCE: Hematology-Oncology Division, Case Western Reserve University School of Medicine, Cleveland, OH, 44106-4937, USA
SOURCE: FASEB J. (2000), 14(15), 2589-2600
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 69
REFERENCE(S): (1) Arends, M; Am J Pathol 1990, V136, P593 HCAPLUS
(2) Asakura, S; J Biochem 1998, V124, P473 HCAPLUS
(3) Asakura, S; J Cell Biol 1992, V116, P465 HCAPLUS
(4) Berrettini, M; Blood 1986, V68, P455 HCAPLUS
(5) Bornstein, P; J Cell Biol 1995, V130, P503 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 24 OF 95 HCAPLUS COPYRIGHT 2001 ACS
TI Cancer treatment using angiopoietins targeted to aminophospholipids
AB Disclosed is the surprising discovery that aminophospholipids, such as phosphatidylserine and phosphatidylethanolamine, are specific, accessible and stable markers of the luminal surface of tumor blood vessels. The present invention particularly provides therapeutic constructs and conjugates that bind to aminophospholipids and contain angiopoietins, and various methods of specifically delivering angiopoietins to the stably-expressed aminophospholipids of tumor blood vessels, thereby exerting anti-tumor effects. The constructs can include binding ligands or antibodies and antibody fragments against the aminophospholipids. Pharmaceutical compns. and kits contg. the targeting agent-angiopoietin constructs are also claimed; both the formulations and kit can also contain a second anticancer agent.
ACCESSION NUMBER: 2001:50517 HCAPLUS
DOCUMENT NUMBER: 134:105841
TITLE: Cancer treatment using angiopoietins targeted to aminophospholipids
INVENTOR(S): Thorpe, Philip E.
PATENT ASSIGNEE(S): Maine Medical Center Research Institute, USA; Board of Regents, the University of Texas System
SOURCE: PCT Int. Appl., 248 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001003735	A1	20010118	WO 2000-US18779	20000711

W: AU, CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1999-143762 P 19990712
REFERENCE COUNT: 4
REFERENCE(S): (1) Godowski; US 6057435 A 2000 HCAPLUS
(2) Maisonpierre, P; Science 1997, V277 HCAPLUS
(3) Thorpe; US 5776427 A 1998 HCAPLUS
(4) Thorpe; US 5855866 A 1999 HCAPLUS

L7 ANSWER 25 OF 95 HCAPLUS COPYRIGHT 2001 ACS

TI **Inhibition** of **angiogenesis** by high-molecular-weight **kininogen** domain 3 peptide analogs

AB Peptide analogs the high-mol.-wt. **kininogen** domain 3 are potent **inhibitors** of **angiogenesis**. The peptides have the formula (a) X1-Asn-Asn-Ala-Thr-Phe-Tyr-Phe-Lys-X2, (b) X3-Cys-Val-Gly-Cys-X4, (c) X5-Leu-Asp-X7-Asn-Ala-Glu-Val-Tyr-X6, or (d) Tyr-Phe-Ile-Asp-Phe-Val-Ala-Arg-Glu-Thr-Thr-X7-Ser-Lys-Glu-Ser (X1-X6 = 0-12 amino acids, more preferably 0-6 amino acids; X7 = Ala, Cys). The peptides may also comprise biol. active fragments of high-mol.-wt. **kininogen** domain 3. Methods of **inhibiting** endothelial cell proliferation and **angiogenesis** are provided.

ACCESSION NUMBER: 2000:420922 HCAPLUS
DOCUMENT NUMBER: 133:68945
TITLE: **Inhibition** of **angiogenesis** by high-molecular-weight **kininogen** domain 3 peptide analogs
INVENTOR(S): McCrae, R. Keith
PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of Higher Education, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035407	A2	20000622	WO 1999-US28465	19991202
WO 2000035407	A3	20000908		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000017494	A1	20000703	AU 2000-17494	19991202

PRIORITY APPLN. INFO.: US 1998-112427 P 19981216
WO 1999-US28465 W 19991202
OTHER SOURCE(S): MARPAT 133:68945

L7 ANSWER 26 OF 95 HCAPLUS COPYRIGHT 2001 ACS

TI **Inhibition** of **angiogenesis** and endothelial cell proliferation by high-molecular-weight **kininogen** and peptide analogs thereof

AB Two-chain high-mol.-wt. **kininogen**, and peptide analogs thereof having homol. to sites within **kininogen** domain 5, are potent **inhibitors** of **angiogenesis**. The peptides have the formula X1-His-Lys-X-Lys-X2 (X = any amino acid; X1, X2= 0-12 amino acids, more preferably 0-6 amino acids, most preferably 0-3 amino acids). X is preferably an amino acid having a nonpolar side chain, or a polar side chain which is uncharged at pH 6.0 to 7.0. X is most preferably Asn, Phe or His. Methods of **inhibiting** endothelial cell proliferation and **angiogenesis** are provided.

ACCESSION NUMBER: 2000:335430 HCAPLUS
DOCUMENT NUMBER: 133:802
TITLE: **Inhibition** of **angiogenesis** and endothelial cell proliferation by high-molecular-weight **kininogen** and peptide analogs thereof
INVENTOR(S): Mccrae, R. Keith

PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of Higher Education, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027866	A1	20000518	WO 1999-US26419	19991105

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-107833 P 19981110
OTHER SOURCE(S): MARPAT 133:802
REFERENCE COUNT: 10
REFERENCE(S): (1) Dennis; US 5830671 A 1998 HCAPLUS
(2) Griffin; US 5756291 A 1998 HCAPLUS
(3) Guerinot; US 5846821 A 1998 HCAPLUS
(4) Heitsch; US 5786365 A 1998 HCAPLUS
(7) Lottspeich; European Journal of Biochemistry 1985, V152, P307 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 27 OF 95 HCAPLUS COPYRIGHT 2001 ACS
TI **Inhibition** of **angiogenesis** by peptide analogs of high-molecular-weight **kininogen** domain 5
AB A method for **inhibition** of endothelial cell proliferation in a mammal comprises peptides and proteins of high-mol.-wt. **kininogen** light chain (domain 5). For example, glutathione-S-transferase (GST) fusion proteins with high-mol.-wt. **kininogen** light chain peptides, i.e. Lys(420)-Ser(513) (SEQ ID NO: 10) and His(441)-Ser(626) (SEQ ID NO: 8), at concns. of 0.27 and 0.39 .mu.M, resp. induced 100% **inhibition** of proliferation of human umbilical vein endothelial cells (HUVEC). Also, GST-SEQ ID NO: 10 at a concn. of 0.27 .mu.M achieved 100% **inhibition** of HUVEC migration to vitronectin.
ACCESSION NUMBER: 2000:335256 HCAPLUS
DOCUMENT NUMBER: 132:343359
TITLE: **Inhibition** of **angiogenesis** by peptide analogs of high-molecular-weight **kininogen** domain 5
INVENTOR(S): Colman, W. Robert; Mousa, A. Shaker
PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of Higher Education, USA; Dupont Pharmaceuticals Company
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027415	A2	20000518	WO 1999-US26377	19991109

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EM, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1044012 A1 20001018 EP 1999-957529 19991109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1998-107844 P 19981110
WO 1999-US26377 W 19991109

L7 ANSWER 28 OF 95 HCAPLUS COPYRIGHT 2001 ACS

TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**

AB We have demonstrated that high mol. wt. **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-assocd. fibrinolysis. We postulated that HK cell binding domains would **inhibit angiogenesis**. We found that recombinant domain 5 (D5) **inhibited** endothelial cell migration toward vitronectin 85% at 0.27 .mu.M with an IC50 (concn. to yield 50% **inhibition**) = 0.12 .mu.M. A D5 peptide, G486-K502, showed an IC50 = 0.2 .mu.M, but a 25-mer peptide from a D3 cell binding domain only **inhibited** migration 10% at 139 .mu.M (IC50 > 50 .mu.M). D6 exhibited weaker **inhibitory** activity (IC50 = 0.50 .mu.M). D5 also potently **inhibited** endothelial cell proliferation with an IC50 = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a mol. homol. model of D5 and designed a series of peptides displaying surface loops. Peptide 440-455 was the most potent (IC50 = 100 nM) in **inhibiting** proliferation but did not **inhibit** migration. D5 **inhibited angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and peptide 400-455 was also **inhibitory** (79%). HK D5 (for which we suggest the designation, "kininostatin") is a potent **inhibitor** of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo.

ACCESSION NUMBER: 2000:55516 HCAPLUS
DOCUMENT NUMBER: 132:164060
TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**
AUTHOR(S): Colman, Robert W.; Jameson, Bradford A.; Lin, Yingzhang; Johnson, Donald; Mousa, Shaker A.
CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA, USA
SOURCE: Blood (2000), 95(2), 543-550
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 52
REFERENCE(S): (1) Asakura, S; J Cell Biol 1992, V116, P465 HCAPLUS

(3) Bacharach, E; Proc Natl Acad Sci U S A 1992, V89, P10686 HCAPLUS
(4) Barnathan, E; Blood 1990, V7 P1795 HCAPLUS
(5) Behrendt, N; J Biol Chem 199., V266, P7842 HCAPLUS
(7) Bradford, H; Blood 1997, V90, P1508 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 29 OF 95 HCAPLUS COPYRIGHT 2001 ACS
TI Biologic activities of the contact factors in vivo. Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis**, and thrombosis
AB A review with 127 refs. is given on the biol. roles of contact factors, particularly the in vivo functions. Bradykinin is released from high mol. wt. prekallikrein (PK) and low mol. wt. **kininogen** (LK) helps to regulate blood pressure under physiol. conditions, whereas in systemic inflammatory response syndrome (SIRS) it is an important contributor to pathol. hypotension. Bradykinin is also important in acute inflammatory disease, but a larger role is played by blood plasma kallikrein, which not only releases bradykinin, but acts directly as an agonist for neutrophils, causing release of elastase, chemotaxis, neutrophil aggregation, and superoxide prodn. New studies involving the contact system interactions with endothelial cells and leukocytes emphasize the role of high mol. wt. **kininogen** (HK) and PK in the initiation of cell-assocd. plasmin formation. HK was also characterized as a counter-adhesive protein, **inhibiting** neutrophil-fibrinogen binding interactions and endothelial adhesion to vitronectin. The domain 5 of HK as well as peptides derived from the domain serve as potent **inhibitors** of **angiogenesis** in vivo, blocking both endothelial cell migration to vitronectin and endothelial cell proliferation. Both clin. (factor XII deficiency) and expt. animal models (**kininogen** deficiency) suggest that HK and/or LK are antithrombotic mols., and that the contact system serves as an anticoagulant, profibrinolytic system. Although FXII, PK, and HK each have multiple domains and functions, the system clearly exists to keep vessels patent, and peptides or recombinant fragments may serve as modulators of blood pressure, inflammation, and fibrinolysis, as well as influencing cell adhesion, **angiogenesis**, and the thrombotic process.
ACCESSION NUMBER: 1999:803232 HCAPLUS
DOCUMENT NUMBER: 132:48325
TITLE: Biologic activities of the contact factors in vivo. Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis**, and thrombosis
AUTHOR(S): Colman, Robert W.
CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, School Medicine, Temple Univ., Philadelphia, PA, 19140, USA
SOURCE: Thromb. Haemostasis (1999), 82(6), 1568-1577
CODEN: THHADQ; ISSN: 0340-6245
PUBLISHER: F. K. Schattauer Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 127
REFERENCE(S): (1) Alfie, M; Biochemical & Biophysical Research Communications 1996, V224(3), P625 HCAPLUS
(3) Asakura, S; J Cell Biol 1992, V116, P465 HCAPLUS
(4) Beutler, B; N Engl J Med 1987, V316, P379 HCAPLUS
(6) Blais, C; Arthritis Rheum 1997, V40, P1327 HCAPLUS
(8) Borkowski, J; Canadian Journal of Physiology &

L7 ANSWER 30 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human high molecular weight **kininogen**. High molecular weight **kininogen** is a 120 kDa glycoprotein which binds with high affinity to endothelial cells, where it is cleaved by plasma kallikrein into heavy and light chains. Analogues of high molecular weight **kininogen** are used in the method of the invention. The specification describes a method of **inhibiting** endothelial cell proliferation. The method comprises contacting endothelial cells with a compound containing high molecular weight **kininogen** analogues. The method and the compounds can be used for **inhibiting** endothelial cell proliferation. The compounds can also be used for **inhibiting angiogenesis**. The compounds can also be used to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93353 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 31 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human high molecular weight **kininogen**. High molecular weight **kininogen** is a 120 kDa glycoprotein which binds with high affinity to endothelial cells, where it is cleaved by plasma kallikrein into heavy and light chains. Analogues of high molecular weight **kininogen** are used in the method of the invention. The specification describes a method of **inhibiting** endothelial cell proliferation. The method comprises contacting endothelial cells with a compound containing high molecular weight **kininogen** analogues. The method and the compounds can be used for **inhibiting** endothelial cell proliferation. The compounds can also be used for **inhibiting angiogenesis**. The compounds can also be used to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93352 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent

LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 32 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human high molecular weight **kininogen**. High molecular weight **kininogen** is a 120 kDa glycoprotein which binds with high affinity to endothelial cells, where it is cleaved by plasma kallikrein into heavy and light chains. Analogues of high molecular weight **kininogen** are used in the method of the invention. The specification describes a method of **inhibiting** endothelial cell proliferation. The method comprises contacting endothelial cells with a compound containing high molecular weight **kininogen** analogues. The method and the compounds can be used for **inhibiting** endothelial cell proliferation. The compounds can also be used for **inhibiting angiogenesis**. The compounds can also be used to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93351 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 33 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human high molecular weight **kininogen**. High molecular weight **kininogen** is a 120 kDa glycoprotein which binds with high affinity to endothelial cells, where it is cleaved by plasma kallikrein into heavy and light chains. Analogues of high molecular weight **kininogen** are used in the method of the invention. The specification describes a method of **inhibiting** endothelial cell proliferation. The method comprises contacting endothelial cells with a compound containing high molecular weight **kininogen** analogues. The method and the compounds can be used for **inhibiting** endothelial cell proliferation. The compounds can also be used for **inhibiting angiogenesis**. The compounds can also be used to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93350 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent

LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 34 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human high molecular weight **kininogen**. High molecular weight **kininogen** is a 120 kDa glycoprotein which binds with high affinity to endothelial cells, where it is cleaved by plasma kallikrein into heavy and light chains. Analogues of high molecular weight **kininogen** are used in the method of the invention. The specification describes a method of **inhibiting** endothelial cell proliferation. The method comprises contacting endothelial cells with a compound containing high molecular weight **kininogen** analogues. The method and the compounds can be used for **inhibiting** endothelial cell proliferation. The compounds can also be used for **inhibiting angiogenesis**. The compounds can also be used to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93349 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 35 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human high molecular weight **kininogen**. High molecular weight **kininogen** is a 120 kDa glycoprotein which binds with high affinity to endothelial cells, where it is cleaved by plasma kallikrein into heavy and light chains. Analogues of high molecular weight **kininogen** are used in the method of the invention. The specification describes a method of **inhibiting** endothelial cell proliferation. The method comprises contacting endothelial cells with a compound containing high molecular weight **kininogen** analogues. The method and the compounds can be used for **inhibiting** endothelial cell proliferation. The compounds can also be used for **inhibiting angiogenesis**. The compounds can also be used to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93348 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent

LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 36 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human high molecular weight **kininogen**. High molecular weight **kininogen** is a 120 kDa glycoprotein which binds with high affinity to endothelial cells, where it is cleaved by plasma kallikrein into heavy and light chains. Analogues of high molecular weight **kininogen** are used in the method of the invention. The specification describes a method of **inhibiting** endothelial cell proliferation. The method comprises contacting endothelial cells with a compound containing high molecular weight **kininogen** analogues. The method and the compounds can be used for **inhibiting** endothelial cell proliferation. The compounds can also be used for **inhibiting angiogenesis**. The compounds can also be used to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93347 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 37 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human high molecular weight **kininogen**. High molecular weight **kininogen** is a 120 kDa glycoprotein which binds with high affinity to endothelial cells, where it is cleaved by plasma kallikrein into heavy and light chains. Analogues of high molecular weight **kininogen** are used in the method of the invention. The specification describes a method of **inhibiting** endothelial cell proliferation. The method comprises contacting endothelial cells with a compound containing high molecular weight **kininogen** analogues. The method and the compounds can be used for **inhibiting** endothelial cell proliferation. The compounds can also be used for **inhibiting angiogenesis**. The compounds can also be used to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93346 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent

LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 38 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
AB The present sequence represents a fragment of the light chain of human high molecular weight **kininogen**. It is used to produce compounds of the invention. High molecular weight **kininogen** is a 120 kDa glycoprotein which binds with high affinity to endothelial cells, where it is cleaved by plasma kallikrein into heavy and light chains. Analogues of high molecular weight **kininogen** are used in the method of the invention. The specification describes a method of **inhibiting** endothelial cell proliferation. The method comprises contacting endothelial cells with a compound containing high molecular weight **kininogen** analogues. The method and the compounds can be used for **inhibiting** endothelial cell proliferation. The compounds can also be used for **inhibiting angiogenesis** . The compounds can also be used to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93345 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 39 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
AB The present sequence represents a fragment of the light chain of human high molecular weight **kininogen**. It is used to produce compounds of the invention. High molecular weight **kininogen** is a 120 kDa glycoprotein which binds with high affinity to endothelial cells, where it is cleaved by plasma kallikrein into heavy and light chains. Analogues of high molecular weight **kininogen** are used in the method of the invention. The specification describes a method of **inhibiting** endothelial cell proliferation. The method comprises contacting endothelial cells with a compound containing high molecular weight **kininogen** analogues. The method and the compounds can be used for **inhibiting** endothelial cell proliferation. The compounds can also be used for **inhibiting angiogenesis** . The compounds can also be used to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93344 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109

PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 40 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
AB The present sequence represents an analogue of the light chain of human high molecular weight **kininogen**. High molecular weight **kininogen** is a 120 kDa glycoprotein which binds with high affinity to endothelial cells, where it is cleaved by plasma kallikrein into heavy and light chains. Analogues of high molecular weight **kininogen** are used in the method of the invention. The specification describes a method of **inhibiting** endothelial cell proliferation. The method comprises contacting endothelial cells with a compound containing high molecular weight **kininogen** analogues. The method and the compounds can be used for **inhibiting** endothelial cell proliferation. The compounds can also be used for **inhibiting angiogenesis**. The compounds can also be used to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93343 peptide DGENE
TITLE: Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109
PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 41 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
AB The present sequence represents the light chain of human high molecular weight **kininogen**. High molecular weight **kininogen** is a 120 kDa glycoprotein which binds with high affinity to endothelial cells, where it is cleaved by plasma kallikrein into heavy and light chains. Analogues of high molecular weight **kininogen** are used in the method of the invention. The specification describes a method of **inhibiting** endothelial cell proliferation. The method comprises contacting endothelial cells with a compound containing high molecular weight **kininogen** analogues. The method and the compounds can be used for **inhibiting** endothelial cell proliferation. The compounds can also be used for **inhibiting angiogenesis**. The compounds can also be used to **inhibit** migration of endothelial cells to vitronectin.
ACCESSION NUMBER: AAY93342 protein DGENE
TITLE: Method for **inhibiting** endothelial cell proliferation, using compound that **inhibit** endothelial cell migration -
INVENTOR: Colman W R; Mousa A S
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(DUPO) DUPONT PHARM CO.
(COLM-I) COLMAN W R.
(MOUS-I) MOUSA A S.
PATENT INFO: WO 2000027415 A2 20000518 41p
APPLICATION INFO: WO 1999-US26377 19991109

PRIORITY INFO: US 1998-107844 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376306 [32]

L7 ANSWER 42 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 peptide derived from high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide, which may optionally include N-terminal and/or C-terminal protecting groups, **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) which are analogues of certain sites in the HK domain 3, in this case amino acids Leu331-Tyr338, and in which cysteine residues may be replaced by alanine residues. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including such peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.
ACCESSION NUMBER: AAY95427 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 43 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of domain 3 of human high mol.wt. **kininogen** (HK). The invention provides peptides (see AAY95405-24) that are analogues of certain sites in the HK domain 3, specifically Asn275-Lys282, Cys246-Cys249, Leu331-Tyr338 and Tyr299-Ser314. The peptides, in which native Cys residues may be replaced by Ala residues, **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.
ACCESSION NUMBER: AAY95426 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell

apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog

INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 44 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Cys246-Cys249. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.
ACCESSION NUMBER: AAY95425 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 45 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a C-terminal fragment of a novel anti-angiogenic D3 peptide (see AAY95416) derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95428). The full-length D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3. The peptides **inhibit** endothelial cell proliferation

and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95424 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 46 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case Tyr299-Ser314, and in which native cysteine residues may be replaced by alanine residues. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present peptide was 28 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.

ACCESSION NUMBER: AAY95423 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 47 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case Tyr299-Ser314, and in which native cysteine residues may be replaced by alanine residues. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95422 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 48 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Leu331-Tyr338, and in which native cysteine residues may be replaced by alanine residues. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis** , **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present peptide was 44 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.

ACCESSION NUMBER: AAY95421 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and

ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 49 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK
domain 3, in this case amino acid residues Leu331-Tyr338, and in which native cysteine residues may be replaced by alanine residues. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present peptide was 42 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.
ACCESSION NUMBER: AAY95420 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell
apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 50 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 peptide derived from high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide, which may optionally include N-terminal and/or C-terminal protecting groups, **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) which are analogues of certain sites in the HK domain 3, in this case amino acids Leu331-Tyr338, and in which cysteine residues

may be replaced by alanine residues. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including such peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95419 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 51 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Leu331-Tyr338, where native cysteine residues may be replaced by alanine residues. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95418 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 52 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

AB The present sequence is that of an N-terminal fragment of a novel anti-angiogenic D3 peptide (see AAY95418) derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The full-length D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95417 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 53 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD

TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

AB The present sequence is that of a D3 peptide derived from high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide, which may optionally include N-terminal and/or C-terminal protecting groups, **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) which are analogues of certain sites in the HK domain 3, in this case amino acids Leu331-Tyr338, and in which cysteine residues may be replaced by alanine residues. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including such peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95416 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 54 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Cys246-Cys249. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present peptide was 30 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.
ACCESSION NUMBER: AAY95415 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 55 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Cys246-Cys249. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used

in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95414 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 56 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a C-terminal fragment of a novel anti-angiogenic D3 peptide (see AAY95414) derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The full-length D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95413 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 57 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -

AB The present sequence is that of an N-terminal fragment of a novel anti-angiogenic D3 peptide (see AAY95414) derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The full-length D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95412 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 58 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 peptide derived from high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide, which may optionally include N-terminal and/or C-terminal protecting groups, **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) which are analogues of certain sites in the HK domain 3, in this case amino acids Cys246-Cys249. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including such peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95411 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216

DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 59 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Asn275-Lys282. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present peptide was less than 0.8 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell proliferation.
ACCESSION NUMBER: AAY95410 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 60 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Asn275-Lys282. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated. The IC50 value for the present peptide was less than 0.8 uM for **inhibition** of fibroblast growth factor-induced HUVEC cell

proliferation.
ACCESSION NUMBER: AAY95409 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 61 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 peptide derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of D3 peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3, in this case amino acid residues Asn275-Lys282. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.
ACCESSION NUMBER: AAY95408 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 62 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a C-terminal fragment of a novel anti-angiogenic D3 peptide (see AAY95408) derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The full-length D3

peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95407 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 63 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of an N-terminal fragment of a novel anti-angiogenic D3 peptide (see AAY95408) derived from human high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The full-length D3 peptide **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) that are analogues of certain sites in the HK domain 3. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including the peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.

ACCESSION NUMBER: AAY95406 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 64 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
AB The present sequence is that of a D3 peptide derived from high mol.wt. **kininogen** (HK) domain 3 (see AAY95426). The D3 peptide, which may optionally include N-terminal and/or C-terminal protecting groups, **inhibits** endothelial cell proliferation and thus possesses anti-angiogenic activity. It is an example of peptides of the invention (see AAY95405-26) which are analogues of certain sites in the HK domain 3, in this case amino acids Asn275-Lys282. The peptides **inhibit** endothelial cell proliferation and may also induce endothelial cell apoptosis. Compositions including such peptides are used in claimed methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation, and inducing endothelial cell apoptosis. Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.
ACCESSION NUMBER: AAY95405 Peptide DGENE
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000035407 A2 20000622 44p
APPLICATION INFO: WO 1999-US28465 19991202
PRIORITY INFO: US 1998-112427 19981216
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-442247 [38]

L7 ANSWER 65 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI A pharmaceutical composition used to **inhibit angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AB The present sequence is derived from human two-chain high molecular weight **kininogen** (HKa) domain 5. HKa is product of high molecular weight **kininogen** (HK) cleavage by plasma kallikrein. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells. Hka or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis.
Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.
ACCESSION NUMBER: AAY81999 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCR[redacted]R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 66 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AB The present sequence is derived from human two-chain high molecular weight **kininogen** (HKa) domain 5. HKa is product of high molecular weight **kininogen** (HK) cleavage by plasma kallikrein. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells. Hka or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting** **angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit** **angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis.
Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.
ACCESSION NUMBER: AAY81998 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 67 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (HKa) by plasma kallikrein. Hka or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting** **angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit** **angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides,

natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY8[redacted]7 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 68 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (HKa) by plasma kallikrein. Hka or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis.

Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81996 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 69 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (HKa) by plasma kallikrein. Hka or a synthetic compound comprising part or all of the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint,

hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81995 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 70 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (HKa) by plasma kallikrein. Hka or a synthetic compound comprising part or all of the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis. Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81994 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 71 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to

two-chain high molecular weight **kininogen** (HKa) by plasma kallikrein. Hka or a synthetic compound comprising part or all of the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis. Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81993 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 72 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (HKa) by plasma kallikrein. Hka or a synthetic compound comprising part or all of the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis. Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81992 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 73 OF 95 DGENE COPYRIGHT 2001 DERWENT INFORMATION LTD
TI A pharmaceutical composition used to **inhibit**

angiogenesis, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

AB The present sequence is derived from human two-chain high molecular weight **kininogen** (HKa) domain 5. HKa is product of high molecular weight **kininogen** (HK) cleavage by plasma kallikrein. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells. Hka or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting** **angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit** **angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis.

Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAB06337 Protein DGENE
TITLE: A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]

L7 ANSWER 74 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**.
AB Cleavage of high molecular weight **kininogen** (HK) by plasma kallikrein results in a light chain and a heavy chain (HK). The light chain has two domains: D6, which binds (pre)kallikrein, and D5, which binds to anionic surfaces, including heparin as well as zinc. Initially, HK was thought to be important for surface-activated coagulation. HKa or D5 binds to the urokinase receptor on endothelial cells, thereby enhancing the conversion of prourokinase to urokinase by kallikrein, and, thus, cell-associated fibrinolysis. HKa or D5 is antiadhesive by competing with vitronectin binding to the urokinase receptor and/or forming a complex with vitronectin. D5 **inhibits** endothelial cell migration, proliferation, tube formation and **angiogenesis**, thus modulating inflammation and neovascularization.
ACCESSION NUMBER: 2001080473 EMBASE
TITLE: Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**.
AUTHOR: Colman R.W.
CORPORATE SOURCE: R.W. Colman, Sol Sherry Thrombosis Research Ctr., Temple University School of Medicine, Philadelphia, PA 19140, United States
SOURCE: Biological Chemistry, (2001) 382/1 (65-70).
Refs: 22
ISSN: 1431-6730 CODEN: BICHF3
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 75 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI IBC's 6th annual conference on **angiogenesis**: Novel therapeutic developments.
AB **Angiogenesis** is a process that is dependent upon co-ordinate production of **angiogenesis** stimulatory and **inhibitory** (angiostatic) molecules. Any imbalance in this regulatory circuit may lead to the development of a number of **angiogenesis**-mediated diseases. **Angiogenesis** is a multi-step process including activation, adhesion, migration, proliferation and transmigration of endothelial cells across cell matrices to or from new capillaries and from existing vessels. **Angiogenesis** is a process involved in the formation of new vessels by sprouting from pre-existing vessels. In contrast, vessel rudiments are sorted by a process termed vasculogenesis. Endothelial heterogeneity and organ specificity might contribute to differences in the response to different anti-angiogenic mechanisms (cultured EC versus microvascular EC isolated from different tissues). Under normal physiological conditions in mature organisms, endothelial cell turnover or **angiogenesis** is extremely slow (from months to years). However, **angiogenesis** can be activated for a limited time in certain situations such as wound healing and ovulation. In certain pathological states, such as human metastasis (oncology) and ocular neovascularisation, disorders including diabetic retinopathy and age-related macular degeneration (ophthalmology), there is excessive and sustained **angiogenesis**. Hence, understanding the mechanisms involved in the regulation of **angiogenesis** could have a major impact in the prevention and treatment of pathological angiogenic processes. Additionally, endothelial cells play a major role in the modelling of blood vessels. The interplay of growth factors, cell adhesion molecules, matrix proteases and specific signal transduction pathways either in the maintenance of the quiescent state or in the reactivation of endothelial cells is critical in physiological and pathological angiogenic processes.
ACCESSION NUMBER: 2001050805 EMBASE
TITLE: IBC's 6th annual conference on **angiogenesis**: Novel therapeutic developments.
AUTHOR: Mousa S.A.
CORPORATE SOURCE: S.A. Mousa, DuPont Pharmaceuticals Co., Wilmington, DE, United States
SOURCE: Expert Opinion on Investigational Drugs, (2001) 10/2 (387-391).
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
012 Ophthalmology
014 Radiology
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 76 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

TI Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: Partial activity within do[redacted]n 5.

AB We previously reported that the binding of two-chain high molecular weight **kininogen** (HKa) to endothelial cells may occur through interactions with endothelial urokinase receptors. Since the binding of urokinase to urokinase receptors activates signaling responses and may stimulate mitogenesis, we assessed the effect of HKa binding on endothelial cell proliferation. Unexpectedly, HKa **inhibited** proliferation in response to several growth factors, with 50% **inhibition** caused by .apprx.10 nM HKa. This activity was Zn2+ dependent and not shared by either single-chain high molecular weight **kininogen** (HK) or low molecular weight **kininogen**. HKa selectively **inhibited** the proliferation of human umbilical vein and dermal microvascular endothelial cells, but did not affect that of umbilical vein or human aortic smooth muscle cells, trophoblasts, fibroblasts, or carcinoma cells. **Inhibition** of endothelial proliferation by HKa was associated with endothelial cell apoptosis and unaffected by antibodies that block the binding of HK or HKa to any of their known endothelial receptors. Recombinant HK domain 5 displayed activity similar to that of HKa. In vivo, HKa **inhibited** neovascularization of subcutaneously implanted Matrigel plugs, as well as rat corneal **angiogenesis**. These results demonstrate that HKa is a novel **inhibitor** of **angiogenesis**, whose activity is dependent on the unique conformation of the two-chain molecule.

ACCESSION NUMBER: 2000436640 EMBASE
TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: Partial activity within domain 5.
AUTHOR: Zhang J.-C.; Claffey K.; Sakthivel R.; Darzynkiewicz Z.; Shaw D.E.; Leal J.; Wang Y.-C.; Lu F.-M.; McCrae K.R.
CORPORATE SOURCE: K.R. McCrae, Hematology-Oncology Division, Case Western Reserve University, School of Medicine, 10900 Euclid Ave., Cleveland, OH 44106-4937, United States. kxm71@po.cwru.edu
SOURCE: FASEB Journal, (2000) 14/15 (2589-2600).
Refs: 69
ISSN: 0892-6638 CODEN: FAJOEC
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 77 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI The hemostatic system as a regulator of **angiogenesis**.
ACCESSION NUMBER: 2000041562 EMBASE
TITLE: The hemostatic system as a regulator of **angiogenesis**.
AUTHOR: Browder T.; Folkman J.; Pirie-Shepherd S.
CORPORATE SOURCE: J. Folkman, Children's Hospital, Hunnewell 103, 300 Longwood Ave., Boston, MA 02115, United States
SOURCE: Journal of Biological Chemistry, (21 Jan 2000) 275/3 (1521-1524).
Refs: 67
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
LANGUAGE: English

L7 ANSWER 78 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-

regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.

AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would **inhibit angiogenesis**. We found that recombinant domain 5 (D5) **inhibited** endothelial cell migration toward vitronectin 85% at 0.27 .mu.M with an IC50 (concentration to yield 50% **inhibition**) =0.12 .mu.M. A D5 peptide, G486-K502, showed an IC50 = 0.2 .mu.M, but a 25-mer peptide from a D3 cell binding domain only **inhibited** migration 10% at 139 .mu.M (IC50 > 50 .mu.M). D6 exhibited weaker **inhibitory** activity (IC50 = 0.50 .mu.M). D5 also potently **inhibited** endothelial cell proliferation with an IC50 = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. Peptide 440-455 was the most potent (IC50 = 100 nM) In **inhibiting** proliferation but did not **inhibit** migration. D5 **inhibited angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and peptide 400-455 was also **inhibitory** (79%). HK D5 (for which we suggest the designation, 'kininostatin') is a potent **inhibitor** of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo.

ACCESSION NUMBER: 2000028682 EMBASE
TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down- regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.
AUTHOR: Colman R.W.; Jameson B.A.; Lin Y.; Johnson D.; Mousa S.A.
CORPORATE SOURCE: R.W. Colman, Sol Sherry Thrombosis Res. Center, Temple University School of Medicine, 3400 North Broad St, Philadelphia, PA 19140, United States. colmanr@astro.temple.edu
SOURCE: Blood, (15 Jan 2000) 95/2 (543-550).
Refs: 52
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 79 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Biologic activities of the contact factors in vivo. Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis** and thrombosis.
ACCESSION NUMBER: 1999423254 EMBASE
TITLE: Biologic activities of the contact factors in vivo. Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis** and thrombosis.
AUTHOR: Colman R.W.
CORPORATE SOURCE: Dr. R.W. Colman, Sol Sherry Thrombosis Res. Center, Temple University School of Medicine, 3400 North Broad Street, Philadelphia, PA 19140, United States. colmanr@astro.temple.edu
SOURCE: Thrombosis and Haemostasis, (1999) 82/6 (1568-1577).

Refs: 127
ISSN: 0340-6245 CODEN: THHADQ
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
037 Drug Literature Index
LANGUAGE: English

L7 ANSWER 80 OF 95 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Kallikrein-kinin in infection and cancer.
AB This review article describes the mechanism of enhancement of vascular permeability in infectious disease and cancer. This phenomenon is primarily mediated by bradykinin, nitric oxide and other unique vascular mediators. They are highly intermingled with each other in these disease states. Furthermore, these mediators are elicited in various in vivo settings most frequently induced by bacterial proteases, and indirect or direct activation of kallikrein-kinin cascade at one or more steps. The key steps involve bacterial proteases or cellular components including lipopolysaccharides. Thus, the use of appropriate protease **inhibitors** or antagonists, or scavengers in the case of nitric oxide, superoxide or peroxynitrite, are anticipated to attenuate the clinical manifestation induced by such mediators. It also explained that fluid accumulation in ascitic or pleural compartments in the case of carcinomatosis in terminal cancer patients can be largely attributed to bradykinin or related mechanism. Systemic bacterial dissemination is also facilitated by bradykinin, or suppressed by kinin antagonists as well as by the **inhibition** of kinin production, respectively. Thus, control of the level of such vascular mediators appears important both in infectious disease and in cancer. .alpha.1-Protease **inhibitor**, which **inhibits** neutrophil elastase, is inactivated by oxidative metabolites such as superoxide and peroxynitrite, and this effect activates matrix metalloproteinases. This indicates that oxidative stress activates proteolytic potential, and thus accelerates the degenerative process upon infection. Copyright (C) 1999 Elsevier Science B.V.
ACCESSION NUMBER: 1999415976 EMBASE
TITLE: Kallikrein-kinin in infection and cancer.
AUTHOR: Maeda H.; Wu J.; Okamoto T.; Maruo K.; Akaike T.
CORPORATE SOURCE: H. Maeda, Department of Microbiology, Kumamoto University, School of Medicine, Honjo 2-2-1, Kumamoto 860-0811, Japan. msmaedah@gpo.kumamoto-u.ac.jp
SOURCE: Immunopharmacology, (1999) 43/2-3 (115-128).
Refs: 47
ISSN: 0162-3109 CODEN: IMMUDP
PUBLISHER IDENT.: S 0162-3109(99)00104-6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
004 Microbiology
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 81 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)
TI Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**
AB Cleavage of high molecular weight **kininogen** (HK) by plasma kallikrein results in a light chain and a heavy chain (HK). The light chain has two domains: D6, which binds (pre)kallikrein, and D5, which binds to anionic surfaces, including heparin as well as zinc. Initially, HK was thought to be important for surface-activated coagulation. HKa or D5 binds to the urokinase receptor on endothelial cells, thereby enhancing

the conversion of prourokinase to urokinase by kallikrein, and, thus, cell-associated fibrinolysis. HKa or D5 is antiadhesive by competing with vitronectin binding to the urokinase receptor and/or forming a complex with vitronectin. D5 **inhibits** endothelial cell migration, proliferation, tube formation and **angiogenesis**, thus modulating inflammation and neovascularization.

ACCESSION NUMBER: 2001:193846 SCISEARCH
THE GENUINE ARTICLE: 406YE
TITLE: Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**
AUTHOR: Colman R W (Reprint)
CORPORATE SOURCE: Temple Univ, Sch Med, Sol Sherry Thrombosis Res Ctr, Philadelphia, PA 19140 USA (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: BIOLOGICAL CHEMISTRY, (JAN 2001) Vol. 382, No. 1, pp. 65-70.
Publisher: WALTER DE GRUYTER & CO, GENTHINER STRASSE 13, D-10785 BERLIN, GERMANY.
ISSN: 1431-6730.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 22
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 82 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)
TI Patent focus on cancer chemotherapeutics. II **angiogenesis** agents: April 2000-September 2000
AB **Angiogenesis** refers to the formation of capillary blood vessels from existing blood vessels: a process that is believed to be critical for tumour growth and metastasis. **Angiogenesis inhibition** represents a new approach to cancer chemotherapy with several agents and approaches non; entering late clinical development. This review summarises the key aspects of recent patent applications referring to **inhibitors** of **angiogenesis** that have been published between April and September 2000. The review covers the main mechanism-based approaches such as MMPI, integrin antagonists, urokinase **inhibitors** and **inhibitors** of the growth factor signalling pathways of fibroblast growth factor (FGF), platelet derived growth factor (PDGF), vascular endothelial growth factor (VEGF) and Tie-2/Tek. Applications referring to endogenous **inhibitors** such as endostatin or angiostatin are also included, as are selected natural products that have data suggesting a link to **angiogenesis** -specific mechanisms of action.

ACCESSION NUMBER: 2001:117935 SCISEARCH
THE GENUINE ARTICLE: 396EC
TITLE: Patent focus on cancer chemotherapeutics. II **angiogenesis** agents: April 2000-September 2000
AUTHOR: Connell R D (Reprint); Beebe J S
CORPORATE SOURCE: Pfizer Corp, Canc Drug Discovery, MS 8118W-B2, Eastern Point Rd, Groton, CT 06340 USA (Reprint); Pfizer Corp, Canc Drug Discovery, Groton, CT 06340 USA
COUNTRY OF AUTHOR: USA
SOURCE: EXPERT OPINION ON THERAPEUTIC PATENTS, (JAN 2001) Vol. 11,
No. 1, pp. 77-114.
Publisher: ASHLEY PUBLICATIONS LTD, UNITEC HOUSE, 3RD FL, 2 ALBERT PLACE FINCHLEY CENTRAL, LONDON N3 1QB, ENGLAND.
ISSN: 1354-3776.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 58
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 83 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)
TI Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: partial activity within domain 5
AB We previously reported that the binding of two-chain high molecular weight **kininogen** (HKa) to endothelial cells may occur through interactions with endothelial urokinase receptors. Since the binding of urokinase to urokinase receptors activates signaling responses and may stimulate mitogenesis, we assessed the effect of HKa binding on endothelial cell proliferation. Unexpectedly, HKa **inhibited** proliferation in response to several growth factors, with 50% **inhibition** caused by similar to 10 nM HKa. This activity was Zn2+ dependent and not shared by either single-chain high molecular weight **kininogen** (HK) or low molecular weight **kininogen**. HKa selectively **inhibited** the proliferation of human umbilical vein and dermal microvascular endothelial cells, but did not affect that of umbilical vein or human aortic smooth muscle cells, trophoblasts, fibroblasts, or carcinoma cells. **Inhibition** of endothelial proliferation by HKa was associated with endothelial cell apoptosis and unaffected by antibodies that block the binding of HK or HKa to any of their known endothelial receptors. Recombinant HK domain 5 displayed activity similar to that of HKa. In vivo, HKa **inhibited** neovascularization of subcutaneously implanted Matrigel plugs, as well as rat corneal **angiogenesis**. These results demonstrate that HKa is a novel **inhibitor** of **angiogenesis**, whose activity is dependent on the unique conformation of the two-chain molecule.
ACCESSION NUMBER: 2000:939227 SCISEARCH
THE GENUINE ARTICLE: 380VD
TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: partial activity within domain 5
AUTHOR: Zhang J C; Claffey K; Sakthivel R; Darzynkiewicz Z; Shaw D
E; Leal J; Wang Y C; Lu F M; McCrae K R (Reprint)
CORPORATE SOURCE: CASE WESTERN RESERVE UNIV, SCH MED, DIV HEMATOL ONCOL, BRB
3, 10900 EUCLID AVE, CLEVELAND, OH 44106 (Reprint); CASE WESTERN RESERVE UNIV, SCH MED, DIV HEMATOL ONCOL, CLEVELAND, OH 44106; CASE WESTERN RESERVE UNIV, SCH MED, DEPT MED, CLEVELAND, OH 44106; UNIV CONNECTICUT, SCH MED, CTR VASC BIOL, DEPT PHYSIOL, FARMINGTON, CT; NEW YORK MED COLL, VALHALLA, NY 10595; DE SHAW & CO INC, NEW YORK, NY; ATTENUON LLC, SAN DIEGO, CA; ABBOTT LABS, DIV PHARMACEUT PROD, DEPT CHEMOTHERAPEUT, ABBOTT PK, IL 60064; ALLEGHENY UNIV HLTH SCI, CTR NEUROVIROL & NEUROONCOL, PHILADELPHIA, PA 19102
COUNTRY OF AUTHOR: USA
SOURCE: FASEB JOURNAL, (DEC 2000) Vol. 14, No. 15, pp. 2589-2600.
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998.
ISSN: 0892-6638.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 69
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 84 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)
TI **Inhibition** of **angiogenesis** by peptides derived from **kininogen** domain 5 & by a monoclonal antibody to **kininogen** domain 5
ACCESSION NUMBER: 2000:150003 SCISEARCH
THE GENUINE ARTICLE: 282GL

TITLE: **Inhibition** of **angiogenesis** by peptides derived from **kininogen** domain 5 & [redacted] monoclonal antibody to **kininogen** domain 5

AUTHOR: Mousa S A (Reprint); Mohamed S; Powell J; Colman R W

CORPORATE SOURCE: DUPONT PHARMACEUT, WILMINGTON, DE; TEMPLE UNIV, SCH MED, SOL SHERRY THROMBOSIS RES CTR, PHILADELPHIA, PA

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, (FEB 2000)

Vol. 35, No. 2, Supp. [A], pp. A295-A296.
Publisher: ELSEVIER SCIENCE INC, 655 AVENUE OF THE AMERICAS, NEW YORK, NY 10010.
ISSN: 0735-1097.

DOCUMENT TYPE: Conference; Journal

FILE SEGMENT: LIFE; CLIN

LANGUAGE: English

REFERENCE COUNT: 0

L7 ANSWER 85 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)

TI **Inhibition** of **angiogenesis** by two-chain high molecular weight **kininogen** (HKa) is associated with induction of endothelial cell apoptosis.

ACCESSION NUMBER: 2000:51161 SCISEARCH

THE GENUINE ARTICLE: 257PH

TITLE: **Inhibition** of **angiogenesis** by two-chain high molecular weight **kininogen** (HKa) is associated with induction of endothelial cell apoptosis.

AUTHOR: Zhang J C (Reprint); Sakthivel R; Lu F M; Darzynkiewicz Z;
McCrae K R

CORPORATE SOURCE: CASE WESTERN RESERVE UNIV, SCH MED, CLEVELAND, OH; ALLEGHENY UNIV HLTH SCI, CTR NEUROVIROL & NEUROONCOL, PHILADELPHIA, PA 19102; NEW YORK MED COLL, VALHALLA, NY 10595

COUNTRY OF AUTHOR: USA

SOURCE: BLOOD, (15 NOV 1999) Vol. 94, No. 10, Part 1, Supp. [1], pp. 36-36.
Publisher: AMER SOC HEMATOLOGY, 1200 19TH ST, NW, STE 300,
WASHINGTON, DC 20036-2422.
ISSN: 0006-4971.

DOCUMENT TYPE: Conference; Journal

FILE SEGMENT: LIFE; CLIN

LANGUAGE: English

REFERENCE COUNT: 0

L7 ANSWER 86 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)

TI Two chain high molecular weight **kininogen inhibits** endothelial cell proliferation and **angiogenesis**: Partial activity within domain

ACCESSION NUMBER: 2000:51156 SCISEARCH

THE GENUINE ARTICLE: 257PH

TITLE: Two chain high molecular weight **kininogen inhibits** endothelial cell proliferation and **angiogenesis**: Partial activity within domain

AUTHOR: Zhang J C (Reprint); Claffey K P; Sakthivel R; Leal J; McCrae K R

CORPORATE SOURCE: CASE WESTERN RESERVE UNIV, SCH MED, CLEVELAND, OH; UNIV CONNECTICUT, SCH MED, FARMINGTON, CT; ABBOTT LABS, ABBOTT PK, IL 60064

COUNTRY OF AUTHOR: USA

SOURCE: BLOOD, (15 NOV 1999) Vol. 94, No. 10, Part 1, Supp. [1], pp. 31-31.

Publisher: AMER SOC HEMATOLOGY, 1200 19TH ST, NW, STE 300,
WASHINGTON, DC 20036-2422.
ISSN: 0006-4971.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L7 ANSWER 87 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)
TI **Inhibition** of tumor **angiogenesis** by a monoclonal antibody to **kininogen** domain
ACCESSION NUMBER: 2000:51154 SCISEARCH
THE GENUINE ARTICLE: 257PH
TITLE: **Inhibition** of tumor **angiogenesis** by a monoclonal antibody to **kininogen** domain
AUTHOR: Colman R W (Reprint); Mousa S A
CORPORATE SOURCE: TEMPLE UNIV, SOL SHERRY THROMBOSIS RES CTR, SCH MED, PHILADELPHIA, PA 19122; DUPONT PHARMACEUT, WILMINGTON, DE
COUNTRY OF AUTHOR: USA
SOURCE: BLOOD, (15 NOV 1999) Vol. 94, No. 10, Part 1, Supp. [1], pp. 29-29.
Publisher: AMER SOC HEMATOLOGY, 1200 19TH ST, NW, STE 300,
WASHINGTON, DC 20036-2422.
ISSN: 0006-4971.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L7 ANSWER 88 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)
TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**
AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (HKa) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding,domains would **inhibit angiogenesis**. We found that recombinant domain 5 (D5) **inhibited** endothelial cell migration toward vitronectin 85% at 0.27 mu M with an IC50 (concentration to yield 50% **inhibition**) = 0.12 mu M A D5 peptide, G486-K502, showed an IC50 = 0.2 mu M, but a 25-mer peptide from a D3 cell binding domain only **inhibited** migration 10% at 139 mu M (IC50 > 50 mu M). D6 exhibited weaker **inhibitory** activity (IC50 = 0.50 mu M) D5 also potently **inhibited** endothelial cell proliferation with an IC50 = 30 nM, while D3 and D6 were inactive, Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. Peptide 440-155 was the most potent (IC50 = 100 nM) in **inhibiting** proliferation but did not **inhibit** migration. D5 **inhibited angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and peptide 400-455 was also **inhibitory** (79%), HK D5 (for which we suggest the designation, ''kininostatin'') is a potent **inhibitor** of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo. (Blood, 2000;95:543-550) (C) 2000 by The American Society of Hematology.
ACCESSION NUMBER: 2000:48248 SCISEARCH
THE GENUINE ARTICLE: 272QG

TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**
AUTHOR: Colman R W (Reprint); Jameson B A; Lin Y Z; Johnson D; Mousa S A
CORPORATE SOURCE: TEMPLE UNIV, SOL SHERRY THROMBOSIS RES CTR, SCH MED, 3400 N BROAD ST, PHILADELPHIA, PA 19140 (Reprint); MCP HAHNEMANN MED SCH, CTR NEUROVIROL, PHILADELPHIA, PA; DUPONT MERCK PHARMACEUT CO, DIV CARDIOVASC, WILMINGTON, DE 19880
COUNTRY OF AUTHOR: USA
SOURCE: BLOOD, (15 JAN 2000) Vol. 95, No. 2, pp. 543-550. Publisher: AMER SOC HEMATOLOGY, 1200 19TH ST, NW, STE 300, WASHINGTON, DC 20036-2422. ISSN: 0006-4971.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 51
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 89 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)
TI Biologic activities of the contact factors in vivo - Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis** and thrombosis
ACCESSION NUMBER: 1999:971544 SCISEARCH
THE GENUINE ARTICLE: 264UN
TITLE: Biologic activities of the contact factors in vivo - Potentiation of hypotension, inflammation, and fibrinolysis, and **inhibition** of cell adhesion, **angiogenesis** and thrombosis
AUTHOR: Colman R W (Reprint)
CORPORATE SOURCE: TEMPLE UNIV, SCH MED, SOL SHERRY THROMBOSIS RES CTR, 3400 N BROAD ST, PHILADELPHIA, PA 19140 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: THROMBOSIS AND HAEMOSTASIS, (DEC 1999) Vol. 82, No. 6, pp. 1568-1577. Publisher: F K SCHATTAUER VERLAG GMBH, P O BOX 10 45 43, LENZHALDE 3, D-70040 STUTTGART, GERMANY. ISSN: 0340-6245.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 126

L7 ANSWER 90 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)
TI Domain 5 of high molecular weight **kininogen** (kininostatin) downregulates endothelial cell proliferation and migration and **inhibits angiogenesis**.
ACCESSION NUMBER: 1999:763940 SCISEARCH
THE GENUINE ARTICLE: 226QX
TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) downregulates endothelial cell proliferation and migration and **inhibits angiogenesis**.
AUTHOR: Colman R W (Reprint); Jameson B; Mousa S A
CORPORATE SOURCE: TEMPLE UNIV, SCH MED, SOL SHERRY THROMBOSIS RES CTR, PHILADELPHIA, PA 19122; DUPONT MERCK PHARMACEUT CO, WILMINGTON, DE 19880; ALLEGHENY UNIV HLTH SCI, PHILADELPHIA, PA 19102

COUNTRY OF AUTHOR: USA
SOURCE: FASEB JOURNAL, (23 APR 1999) Vol. No. 7, Supp. [S], p. A1407-A1407.
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998.
ISSN: 0892-6638.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 0

L7 ANSWER 91 OF 95 SCISEARCH COPYRIGHT 2001 ISI (R)
TI **Inhibition** of **angiogenesis** by peptides derived from **kininogen.**
ACCESSION NUMBER: 1999:1270 SCISEARCH
THE GENUINE ARTICLE: 141AW
TITLE: **Inhibition** of **angiogenesis** by peptides derived from **kininogen.**
AUTHOR: Colman R W (Reprint); Lin Y; Johnson D; Mousa S A
CORPORATE SOURCE: DUPONT MERCK PHARMACEUT CO, WILMINGTON, DE 19880; TEMPLE UNIV, SCH MED, SOL SHERRY THROMBOSIS RES CTR, PHILADELPHIA, PA 19122
COUNTRY OF AUTHOR: USA
SOURCE: BLOOD, (15 NOV 1998) Vol. 92, No. 10, Part 1, Supp. [1], pp. 701-701.
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399.
ISSN: 0006-4971.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L7 ANSWER 92 OF 95 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
TI **Inhibiting angiogenesis** in a mammal using an antibody against high molecular weight **kininogen** domain 5.
AN 2001-328940 [34] WPIDS
AB WO 200134195 A UPAB: 20010620
NOVELTY - **Inhibiting angiogenesis** or tumor growth or formation in a mammal, comprising administering an antibody (Ab1) against an antigenic determinant of high molecular weight **kininogen** domain 5 (HMWKd5), is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for **inhibiting** endothelial cell proliferation, comprising contacting endothelial cells with Ab1.
ACTIVITY - Cytostatic; antidiabetic; ophthalmological; antirheumatic; antiarthritic; antiatherosclerotic.
A chicken chorioallantoic neovascularization assay was performed to determine the **inhibition** of **angiogenesis** by antibody MabC11C1, the product of hybridoma ATCC HB-8964. In 10 day old chicken embryos a small hole was made in the shell concealing the air sac and a second hole directly over an avascular portion of the embryonic membrane. A false air sac was created beneath the second hole using negative pressure to the first hole which caused the chorioallantoic membrane (CAM) to separate from the shell. A 1 cm2 window was cut in to the shell over the dropped CAM and sterilized Whatman number 1 filter disks adsorbed with fibroblast growth factor (FGF)-2 (Life technologies) in phosphate buffered saline (PBS) at 1 micro g/ml were placed on the growing CAMs. A range of Mab concentrations in 25 micro liter buffered saline was applied to the saturated filter 24 hours later. CAM tissue beneath the filter was

resected from embryos 48 hours post treatment. Sections were examined under a SV6 stereo croscope at 50x magnification. e number of vessel branch points cont ed in a circular region equal the area of a filter
disk was counted for each section. Results showed that MabC11C1 **inhibited** the FGF-2 stimulated neovascularization by 71.3%.

MECHANISM OF ACTION - Antibody therapy.

USE - The invention is used to **inhibit** endothelial cell proliferation, vascular tube formation and/or neovascularization in disease states such as diabetic retinopathy, rheumatoid arthritis and atherosclerotic plaques and during tumor growth.

Dwg.0/8

ACCESSION NUMBER: 2001-328940 [34] WPIDS
DOC. NO. CPI: C2001-100961
TITLE: **Inhibiting angiogenesis** in a mammal using an antibody against high molecular weight **kininogen** domain 5.
DERWENT CLASS: B04 D16
INVENTOR(S): COLMAN, R W; MOUSA, S A
PATENT ASSIGNEE(S): (DUPO) DUPONT PHARM CO; (UTEM) UNIV TEMPLE
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001034195	A1	20010517	(200134)*	EN	19

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001034195	A1	WO 2000-US30975	20001110

PRIORITY APPLN. INFO: US 1999-165165 19991112

L7 ANSWER 93 OF 95 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Treating vascularized tumors using constructs comprising angiopoietins which bind to stably-expressed aminophospholipids of tumor blood vessels.
AN 2001-081048 [09] WPIDS
AB WO 200103735 A UPAB: 20010213

NOVELTY - Therapeutic constructs and conjugates that bind to aminophospholipids and contain angiopoietins, and methods of delivering those angiopoietins to stably-expressed aminophospholipids of tumor blood vessels for the treatment of cancer (e.g. vascularized tumors), are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a binding ligand (I) comprising a targeting agent that binds to an aminophospholipid operatively attached to an angiopoietin;

(2) an antibody construct (II), comprising an anti-aminophospholipid antibody or antigen binding fragment operatively attached to an angiopoietin;

(3) a kit (III) comprising a targeting agent -angiopoietin construct that comprises a targeting agent that binds to an aminophospholipid operatively attached to an angiopoietin and:

(a) a targeting agent-detectable agent construct that comprises a second targeting agent that binds to an aminophospholipid operatively attached to a detectable agent; and/or

(b) a second anticancer agent;

(4) a method (IV) for treating an animal having a vascularized tumor,

comprising administering a binding ligand that comprises an angiopoietin operatively attached to a targeting agent that binds to an aminophospholipid on the luminal surface of blood vessels of a vascularized tumor;

(5) a method (V) for inducing tumor regression, comprising administering to an animal (which has a vascularized tumor), a binding ligand that induces regression in the tumor blood vessels (the binding ligand comprises angiopoietin-2 operatively attached to a targeting agent that binds to an aminophospholipid expressed on the luminal surface of blood vessels of the vascularized tumor); and

(6) a method (VI) for **inhibiting** tumor growth, comprising administering to an animal (which has a vascularized tumor), a binding ligand that **inhibits** the growth of the tumor blood vessels (the binding ligand comprises angiopoietin-1 operatively attached to a targeting agent that binds to an aminophospholipid expressed on the luminal surface of blood vessels of the vascularized tumor).

ACTIVITY - Cytostatic.

Male CB17 SCID (severely combined immunodeficiency) mice were injected subcutaneously with 1 multiply 107 L540 tumor cells. when the tumors had reached a volume of 0.4-0.6 cm3, the mice were injected intravenously with either 4 micro g tTF (truncated tissue factor), 20 micro g of anti-VCAM-1.tTF, 16 micro g anti-VCAM-1 antibody, a mixture of 6 micro g of anti-VCAM-1 antibody and 4 micro g of tTF, 20 micro g control IgG.tTF or saline.

Mice were sacrificed when tumors reached a volume of 2 cm3 (or earlier if they showed necrosis or ulceration).

Mean tumor volume of anti-VACM-1.tTF treated mice was significantly reduced after 21 days of treatment in comparison to all other groups. Nine out of 15 mice treated with the specific coaguligand showed more than 50% reduction in tumor volume. The effect was specific as un-conjugated tTF, control IgG coaguligand and mixtures of free anti-VCAM-1 antibody and tTF did not affect tumor growth.

MECHANISM OF ACTION - **Inhibition** of tumor **angiogenesis**.

USE - The constructs, conjugates and methods ((I)-(VI)) may be used for the treatment of cancers, especially vascularized tumors, and for preventing **angiogenesis** with in cancerous tissue.

Dwg.0/4

ACCESSION NUMBER: 2001-081048 [09] WPIDS
DOC. NO. CPI: C2001-023403
TITLE: Treating vascularized tumors using constructs comprising angiopoietins which bind to stably-expressed aminophospholipids of tumor blood vessels.
DERWENT CLASS: B04 D16
INVENTOR(S): THORPE, P E
PATENT ASSIGNEE(S): (MAIN-N) MAINE MEDICAL CENT RES INST; (TEXA) UNIV TEXAS SYSTEM
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001003735 A1		20010118	(200109)*	EN	245
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP US					
AU 2000062081 A		20010130	(200127)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001003735 A1		WO 2000-US18779	20000711
AU 2000062081 A		AU 2000-62081	20000711

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000062081 A	Based on	WO 200103735

PRIORITY APPLN. INFO: US 1999-143762 19990712

L7 ANSWER 94 OF 95 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
TI Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog.
AN 2000-442247 [38] WPIDS
AB WO 200035407 A UPAB: 20000811
NOVELTY - A pharmaceutical composition comprising a compound of 8 to 32 amino acids (A) that is a **kininogen** domain 3 analog and optionally contains an amino-terminal and/or carboxy-terminal protecting group.

DETAILED DESCRIPTION - The pharmaceutical composition comprises a compound with the formula X1 Asn Asn Ala Thr Phe Tyr Phe Lys X2, (A) where X1 and X2 are from zero to twelve amino acids.

INDEPENDENT CLAIMS are also included for the following:

(1) A pharmaceutical composition comprising a compound with the formula X3 Cys Val Gly Cys X4 (B), where X3 and X4 are zero to twelve amino acids. A disulfide bond between the cysteine residues of the segment Cys Val Gly Cys and an amino-terminal and/or carboxy-terminal protecting group are optionally present;

(2) A pharmaceutical composition comprising a compound with the formula X5 Leu Asp X7 Asn Ala Glu Val Tyr X8 (C), where X5 and X6 are zero to twelve amino acids, X7 is Ala or Cys, and the compound optionally contains an amino-terminal and/or carboxy-terminal protecting group;

(3) A pharmaceutical composition comprising a peptide fragment of high molecular weight **kininogen** domain 3 or an analog where cysteine residues are replaced by alanine residues that **inhibits** endothelial cell proliferation. The fragment optionally contains an amino-terminal and/or carboxy-terminal protecting group;

(4) **Inhibiting angiogenesis** comprising administering to a mammal the new composition;

(5) **Inhibiting** endothelial cell proliferation comprising administering to a mammal the new composition;

(6) Inducing endothelial cell apoptosis comprising administering to a mammal the new composition;

(7) **Inhibiting** endothelial cell proliferation comprising contacting endothelial cells with a compound of formula (A), (B) or (C);

(8) **Inhibiting** endothelial cell proliferation comprising contacting endothelial cells with a peptide fragment of high molecular weight **kininogen** domain 3 or an analog where cysteine residues are replaced by alanine residues. The compound optionally contains an amino-terminal and/or carboxy-terminal protecting group.

ACTIVITY - Anti-angiogenic; Cytostatic; Antirheumatic; Antiarthritic; Ophthalmological. The median **inhibitory** concentrations for 6 of the claimed sequences were less than 0.8 to 28 micro M for fibroblast growth factor-induced endothelial cell proliferation of 30000 cells/ml

human umbilical vein endothelial cells.
MECHANISM OF ACTION - **Kininogen** domain 3 anal
USE - The new composition is used to **inhibit** **angiogenesis, inhibit** endothelial cell proliferation or induce endothelial cell apoptosis (claimed). Cancer, rheumatoid arthritis, and ocular disorders characterized by undesired vascularization of the retina are treated.
Dwg.0/0

ACCESSION NUMBER: 2000-442247 [38] WPIDS
DOC. NO. CPI: C2000-134415
TITLE: Composition for **inhibiting angiogenesis** and endothelial cell proliferation, inducing endothelial cell apoptosis and treating cancer, rheumatoid arthritis, and ocular disorders comprises a **kininogen** domain 3 analog.
DERWENT CLASS: B04 D16
INVENTOR(S): MCCRAE, R K
PATENT ASSIGNEE(S): (MCCR-I) MCCRAE R K; (UTEM) UNIV TEMPLE
COUNTRY COUNT: 89
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000035407	A2	20000622	(200038)*	EN	44
AU 2000017494	A	20000703	(200046)		

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000035407	A2	WO 1999-US28465	19991202
AU 2000017494	A	AU 2000-17494	19991202

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000017494	A Based on	WO 200035407

PRIORITY APPLN. INFO: US 1998-112427 19981216

L7 ANSWER 95 OF 95 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
TI A pharmaceutical composition used to **inhibit** **angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis.
AN 2000-376483 [32] WPIDS
AB WO 200027866 A UPAB: 20000706
NOVELTY - A pharmaceutical composition used to **inhibit** **angiogenesis, inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis, is new.
DETAILED DESCRIPTION - A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of the formula (I) and optionally comprises an amino terminal and/or carboxy terminal protecting group, is new:
(I) X1-His-Lys-X-Lys-X2;
X = any amino acid;

X1 = 0-12 amino acids; and
X2 = 0-12 amino acids.
INDEPENDENT CLAIMS are also included for:
(1) a method of **inhibiting angiogenesis** comprising administering to a mammal an effective amount of (I);
(2) a method of **inhibiting** endothelial cell proliferation comprising administering to a mammal an effective amount of (I);
(3) a method of inducing endothelial cell apoptosis comprising administering to a mammal an effective amount of (I);
(4) a method of **inhibiting angiogenesis** comprising administering to a mammal an effective amount of two-chain high molecular weight **kininogen**;
(5) a method of **inhibiting** endothelial cell apoptosis comprising administering to a mammal an effective amount of two-chain high molecular weight **kininogen**;
(6) a method of **inhibiting angiogenesis** comprising administering to a mammal an effective amount of single chain high molecular weight **kininogen**;
(7) a method of **inhibiting** endothelial cell proliferation comprising contacting endothelial cells with (I); and
(8) a compound of formula (i) and optionally comprising an amino terminal and/or carboxy-terminal protecting group. :
(i) X1-His-Lys-X-Lys-X2:
X1 = His-Gly-His-Glu-Gln-Gln-His-Gly-Leu-Gly-His-Gly or N-terminal truncation fragment thereof containing at least one amino acid;
X2 = 0 amino acids or the segment Leu-Asp-Asp-Asp-Leu-Glu-His-Gln-Gly-Gly-His-Val, or C-terminal truncation fragment thereof containing at least one amino acid.
ACTIVITY - None given.
MECHANISM OF ACTION - None given.
USE - (I), a two-chain high molecular weight **kininogen**, or a single chain high molecular weight **kininogen** can be used in methods for **inhibiting angiogenesis**, **inhibiting** endothelial cell proliferation and for inducing endothelial cell apoptosis (claimed).
ADVANTAGE - None given.
Dwg.0/8

ACCESSION NUMBER: 2000-376483 [32] WPIDS
DOC. NO. NON-CPI: N2000-282694
DOC. NO. CPI: C2000-113885
TITLE: A pharmaceutical composition used to **inhibit angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): MCCRAE, R K
PATENT ASSIGNEE(S): (MCCR-I) MCCRAE R K; (UTEM) UNIV TEMPLE
COUNTRY COUNT: 89
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000027866	A1	20000518	(200032)*	EN	52

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000019106 A 20000529 (200041)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000027866	A1	WO 1999-US26419	19991105
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AU 2000019106	A	Based on	WO 200027866

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